Exploration and Implementation of Augmented Reality for External Beam Radiotherapy

Thesis submitted in accordance with the requirements of the University of Chester for the degree of Doctor of Philosophy

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Abstract

Title of the Thesis:

Exploration and Implementation of Augmented Reality for External Beam Radiotherapy

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We have explored applications of Augmented Reality (AR) for external beam radiotherapy to assist with treatment planning, patient education, and treatment delivery.

We created an AR development framework for applications in radiotherapy (RADiotherapy Augmented Reality, RAD-AR) for AR ready consumer electronics such as tablet computers and head mounted devices (HMD).

We implemented in RAD-AR three tools to assist radiotherapy practitioners with: treatment plans evaluation, patient pre-treatment information/education, and treatment delivery.

We estimated accuracy and precision of the patient setup tool and the underlying self-tracking technology, and fidelity of AR content geometric representation, on the Apple iPad tablet computer and the Microsoft HoloLens HMD. Results showed that the technology could already be applied for detection of large treatment setup errors, and could become applicable to other aspects of treatment delivery subject to technological improvements that can be expected in the near future.

We performed user feedback studies of the patient education and the plan evaluation tools. Results indicated an overall positive user evaluation of AR technology compared to conventional tools for the radiotherapy elements implemented.

We conclude that AR will become a useful tool in radiotherapy bringing real benefits for both clinicians and patients, contributing to successful treatment outcomes.

The material being presented for examination is my own work and has not been submitted for an award of this or another HEI except in minor particulars which are explicitly noted in the body of the thesis. Where research pertaining to the thesis was undertaken collaboratively, the nature and extent of my individual contribution has been made explicit.

Francesco Cosentino:
Date:

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Table of Contents

Chapter 1. Motivation

In this PhD research project, we have investigated potential benefits arising from application of augmented reality (AR) technology in external beam radiotherapy (RT). We considered applications to treatment planning and delivery, and to aid discussion with patients

We have created RAD-AR (RADiotherapy - Augmented Reality), a software framework for applications of Augmented Reality in Radiotherapy. RAD-AR allows development of applications sharing the same user interface and advanced visualization philosophy. We have investigated some performance and usage aspects of three applications based on RAD-AR.

1.1 Background

1.1.1 Virtual Reality, Augmented Reality, and Mixed Reality

Whereas a virtual reality (VR) system creates an entirely computer-generated virtual scene (Burdea & Coiffet, 2003), when the computer-generated content, such as 3D graphics, is mixed with a direct view of the real scene we talk of augmented reality (AR) (Craig, 2013). AR lets the user see the real world while also seeing virtual objects anchored to a point in real space; from the perspective of the person who lives the AR experience the virtual objects can be visually perceived as real, with the view seen by the user changing in the same way as if the virtual content was a physical object present in the scene.

Recently, a terminological distinction is becoming popular in part of the scientific community. What we defined above as AR is sometimes called Mixed Reality (MR), whereas AR is used with a narrower meaning to indicate the addition of digital information and data as labels or virtual cards, etc., on top of the perception of the real world. This is, for example, the accepted terminology in the Microsoft HoloLens (one of the latest AR hardware devices to become available) developers community (“Replacing VR and AR with ‘mixed reality’”, n.d.). The scientific community mainly refers to Milgram (Milgram & Kishino, 1994), where the authors define mixed reality as “anywhere between the extrema of the virtuality continuum”

(Figure 1), and refers to AR in the way we defined it; augmented virtuality (AV) is defined as the situation where the real content is embedded in a virtual environment.

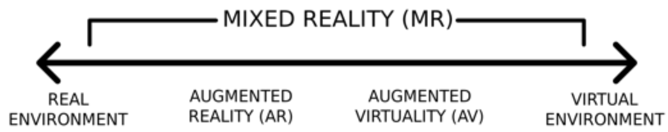


Figure 1 The virtual continuum (from (Milgram & Kishino, 1994)**)**

Being a matter of definitions, and considering the fact that the prominent trend in the scientific community is to talk about AR in the way we defined it at the beginning of this section, we will adhere to Milgram's definition.

AR systems often generate a 3D perception for the user, but more generally, the perception of the scene can also include audio or even touch, for example, using haptic force feedback. 3D perception can be generated by stereoscopic methods or holographic methods.

Stereoscopic methods combine two different views of the scene from the two positions corresponding to the observer's left and right eye so that each eye can see its own view only. The human brain will then generate a spatial perception of the scene from these two views. In recent years many researchers have been working on 3D displays in various fields, including: military, industry, medicine, computer games, and entertainment. A head mounted display (HMD) is a particular type of stereoscopic device where the left and right images are positioned on displays immediately in front of the wearer's eyes. When used for AR, a HMD can be categorised as either optical see-through or video see-through. Video see-through systems use video feeds from cameras inside head-mounted devices to visualize the real environment. Optical see-through systems combine computer-generated imagery with a direct view of the real world; the user can see what is shown on a glass screen while still being able to see through it. The major technologies usually exploited are: LCD (liquid-crystal display), and LED (light-emitting diode) or OLED (organic light-emitting diode); LCD systems impose a pattern of shading and colours on the background seen through the display, while LED or OLED systems impose a glowing image pattern on the background. For a comprehensive comparison between video see-through and optical see-through systems we refer to (Rolland & Fuchs, 2000)(Medeiros, Sousa, Mendes, Raposo, & Jorge, 2016). Video see-through systems have the advantage, over optical see-through systems, of matching the video latency (i.e. delay) with the computer graphics latency. Latency is inherent to immersive imaging systems, as computer graphic generation is not immediate and motion trackers are not instantaneous; even when refreshing images at 120 Hz, there is a perceivable lag from user motion sensing to imaging. When computer graphics need to be overlaid on to the real scene, optical see through offers no latency for the real scene, but there is a latency affecting the graphics. In contrast, using video see-through allows perfect synchronization of real scene video and augmented content graphics.

Another technology to generate 3D perception can be adopted: the holographic technique (Onural, Yaraş, & Hoonjong Kang, 2011). The 3D element is implemented into the image display mechanism itself (e.g., the physical visualisation of image voxels is generated at different depths inside the device). Devices using the holographic technique are generally based on highly specialized hardware and are more expensive than stereoscopic displays.

Despite the relatively high cost of both stereoscopic and holographic systems, work has been done to investigate the benefits of AR on both platforms at different stages of the radiotherapy treatment process. In recent years, the cost aspect and availability on the consumer electronics market is rapidly changing. For example, in March 2016 Microsoft released the HoloLens (developer edition), an HMD considered at the time of writing one of the state-of-the art systems in AR. The HoloLens follows an innovative design philosophy (Kress & Cummings, 2017), featuring a tinted visor with two transparent combiner lenses; projected images are displayed on the visor's lower half. These dual lenses use optical waveguides to colour red, green, and blue through three diffractive layers. A "light engine" above each combiner lens projects light into the lens (Figure 2). The coloured light ray then hits a diffractive element and is reflected repeatedly along a layer until it is outputted from the lens. The images are formed in the user's field of view rather than projected into the user's eyes (Rauschnabel & Ro, 2016). The result is that two different images can be produced in front of each lens in the user's field of view, and because each eye sees a different image, three-dimensional viewing can be created. The optical system break down is as follows:

microdisplay → imaging optics → waveguide → combiner → gratings.

More detail can be found in ("AR/MR Combiners Part 2 – Hololens | Karl Guttag on Technology," 2017). The Microsoft HoloLens in its developer edition costs at the time of writing about £2,700; combining the latest VR HMDs with a camera can produce a video see through device for around £500. This will encourage greater use of AR technology in radiotherapy and other medical fields. AR applications can also be implemented on smartphone and tablet devices, greatly reducing hardware related costs.

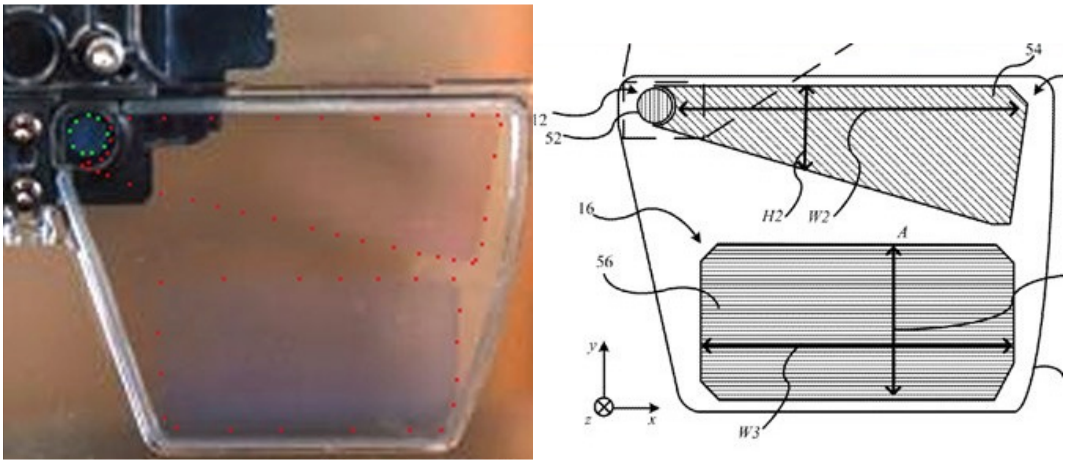


Figure 2 HoloLens light engine (from ("AR/MR Combiners Part 2 – Hololens," 2017)**)**

In computer applications development, AR represents also a novel user interface paradigm, as opposed to WIMP (Windows-Icons-Menus-Pointer paradigm) (Hollerer & Hans, 2004). AR is largely investigated in the domain of human-computer interaction (HCI) (Koelle, Lindemann, Stockinger, & Kranz, 2014)(Stephanidis, 2014), where headsets, handheld, or wearable devices enable the user to move in the real environment, receiving at the same time continuous information from computer systems, presented to the user as virtual content anchored to the real environment. Considering the evolution of HCI in relation to medicine, three new generation mass-produced types of devices, widely available and relatively low cost, show the potential (and in part have already started) to modify how we interact with clinical data:

- tablet computers (Microsoft Surface, Apple iPad, Samsung Galaxy, Asus ZenPad, Google Pixel, etc.);
- VR HMDs (Samsung Gear VR, Google Cardboard and DayDream, HTC Vive, Oculus Rift, etc.);

- AR HMDs (Microsoft HoloLens, Epson Moverio, Metavision Meta, etc.).

With respect to using a 2D display device to look at 3D data, AR and VR have the advantage to offer the user more intuitive perception of geometric and positional details. In AR the real environment is constantly visible, providing a natural geometric reference, and interaction can happen by gestures in the physical space as if the virtual content is physically present. The direct view of the environment is excluded in VR, but, if the system is correctly calibrated, the completely virtual environment perceived by the user reproduces the visual perception of a real environment in all its spatial and dimensional aspects, providing perceptual background for natural and intuitive geometric perception of 3D data.

In contexts where viewing the physical environment is not essential, e.g. for medical imaging visualization by clinicians, VR could adequately cover some applications of AR. However, AR could have an advantage over VR in typical situations where collaboration of several specialists is required, e.g. for a team of radiotherapy professionals discussing and evaluating a treatment plan. Using an AR system to visualize the treatment plan would have the advantage, over a VR system, that communication between different users, like gestures pointing at aspects of the treatment plan, or body language accompanying verbal communication, will be direct, with no mediation through avatars (in computing, an avatar is the graphical representation of the user or the user's character), as it would otherwise be required in a VR system (Lok, Naik, Whitton, & Brooks, 2003). Potential advantages of AR over VR arising from the possibility to see and interact naturally with other people have been discussed in the literature (e.g. (Kaufmann, 2003)). Another situation in which AR has a clear advantage over VR is when the patient needs to be physically present as part of the process, e.g. when the radiotherapy treatment is delivered or when the patient is medically examined.

In some domains, e.g. surgery and architecture, systems allowing deployment of AR applications based on a coherent framework to all the main aspects of the discipline (e.g. planning, implementation, and education/information phases) are appearing on the market. AR visualization of 3D radiological images for surgical procedures has been described as applicable to the following aspects (Courtier, 2017), ("Medical Augmented Reality", 2017):

- understanding complicated anatomy before surgery in the planning phase

- roadmapping for important structures during surgery
- education of patients about their surgeries.

In the architecture domain, comprehensive applications of AR have been considered ("4 Ways Virtual and Augmented Reality," 2017), covering:

- planning phase
- delivery of work instructions to builders
- presentation of models to customers.

1.1.2 Overview of Radiotherapy

Radiotherapy is the treatment of disease, usually cancer, with ionizing radiation (Khan, 2014). A linear accelerator (LINAC) is the device most commonly used for external beam radiotherapy treatments. Radiotherapy is a complex process with traditionally two distinct phases: treatment planning and treatment delivery.

Treatment Planning

When a patient is prescribed external beam radiotherapy a planning CT scan of the relevant patient anatomy is acquired. Subsequently, a treatment plan to deliver the prescribed radiation dose is produced. The primary goal of radiotherapy treatment planning is to design a set of ionizing radiation beams that deliver high doses to the tumour while minimizing dose to healthy tissue and vital organs. Healthy tissue should ideally receive the minimum possible dose, but although treatment planning tries to minimize the dose delivered to healthy tissues irradiating the cancer from different directions all focussing on the disease, some radiation is also absorbed by healthy tissues and healthy tissue is damaged, producing side effects with different degrees of risk.

With dedicated computer simulation software, the patient imaging data is used to iteratively determine the optimal radiation beam orientations and beam shapes with; the outcome is a planned radiation dose distribution in the patient around a target volume. The efficient design and final choice of the optimal treatment plan remains a non-trivial task as the radiotherapy professional needs to be able to visualize and understand the dose coverage of anatomic structures in 3D, and increasingly 4D if reproducibility and time effects are included. Therefore accurate and informative 3D visualization is required for intuitive and quick evaluation of competing plans. The wealth of information made available by the development of imaging modalities requires efficient processing by the treatment team to deliver high quality care. This is where computer graphics (CG) and advanced information visualization techniques become useful (Vidal et al., 2006).

Although the 2D monitors used in conventional radiotherapy planning systems allow for displaying 3D images of the dose distribution together with patient anatomy data, typically only 2D flat surfaces are used. Treatment planners usually view patient anatomy slice-by-slice, in three orthogonal planes (axial, sagittal, and coronal), showing images from different modalities side-by-side or using relatively simple overlays (Figure 3).

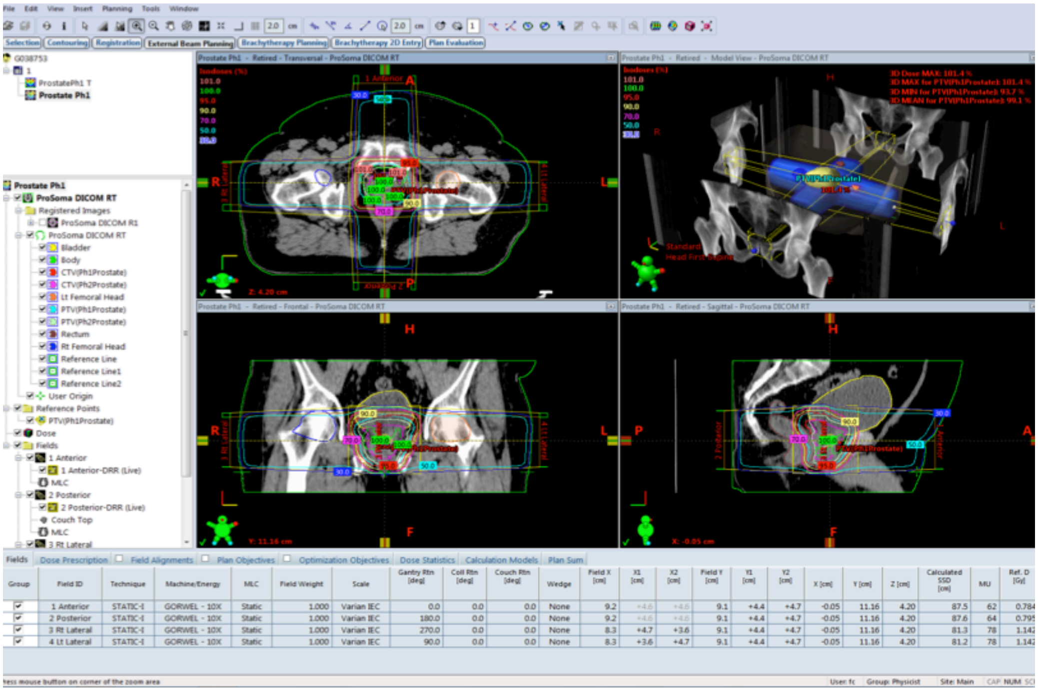


Figure 3 Treatment Planning System. Four-fields prostate treatment plan. The four radiation beams intersect in the prostate Planning Target Volume (PTV). The four image frames show transverse (top-left), coronal (bottom-left), and sagittal (bottom-right) views of the CT dataset, organ outlines, and dose distribution. A 3D view of treatment beams and volumes is shown in the top-right part. Parameters for beam geometry and dose information are displayed in the bottom frame. The left frame shows logical grouping of information and allows switching on/off visualization of dose distribution, treatment beams, and organ outlines. Menus at the top allow design, calculation, optimization, and evaluation of treatment plans, other than import/export and other data operations.

Treatment Delivery

The total radiation dose, split into a number of dose delivery sessions (fractions), and the number of fractions, are prescribed by the clinician and delivered according to clinical protocols (Halperin, Brady, Wazer, & Perez, 2013).

The planning CT scan is acquired on a scanner (Figure 4, top) equipped with a couch reproducing the LINAC treatment couch, and a laser pointing system matched to the one installed in the treatment room (Figure 4, bottom).

Since the treatment plan is based on the planning CT scan, in order to accurately deliver the planned dose the patient position on the CT scan couch has to be reproduced on the treatment (LINAC) couch (Zelefsky et al., 1997). Patient positioning is traditionally based on laser alignment with skin markers, and treatment room imaging for verification (Figure 4).

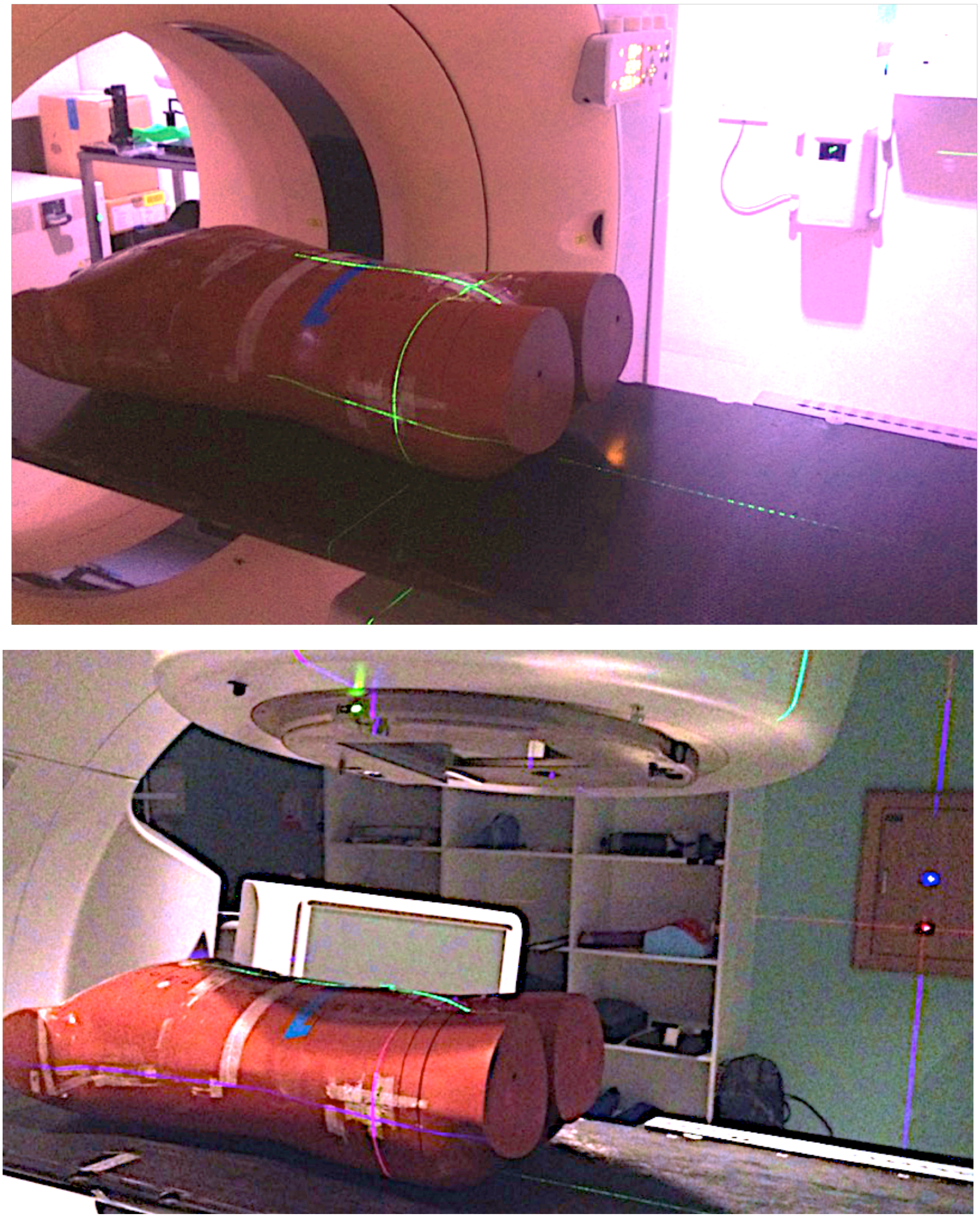


Figure 4 RANDO radiotherapy quality control anthropomorphic phantom (Imaging Solutions, AU) on the planning CT scammer couch (top) and on the treatment couch (bottom). Matched laser pointing systems are fitted in the CT scanner and the LINAC rooms allowing setup the patient in the same position on both the planning CT scanner couch and the treatment couch.

Other techniques can be used to improve patient positioning accuracy such as implantation of radio-opaque fiducial markers in to the prostate or projection of light patterns on to the patient body. The main challenge is to ensure that, for each fraction of the treatment (up to 35 daily visits), the dose delivered to the patient is as close as possible to the planned dose, taking into account body and organ variations. These occur for a host of reasons, of which internal motion due to breathing and tumour shrinkage due to treatment are examples. A number of commercial systems for treatment setup rely on 3D vision technology to capture the patient's body shape on the treatment couch, and compare it with the planning scan, highlighting significant differences (Krengli et al., 2009)("humediQ," 2018)("Advanced radio therapy," 2018).

More recently, diagnostic quality images acquired in the treatment room immediately prior to treatment to check patient setup have become available for treatment machines equipped with kV imaging panels and Cone-Beam CT (CBCT) facilities (Jaffray, Siewerdsen, Wong, & Martinez, 2002). In routine clinical practice typically 10 to 15 minutes treatment slots are scheduled daily for each patient. To maintain this workflow, the increasing wealth of imaging information made available from new technologies immediately before and during treatment needs to be quickly processed by the treatment team. AR techniques have much potential in this respect where they can help to make an optimal use of the setup verification images, improve accuracy of patient positioning, or speed up the patient positioning decisions enabling fast but accurate treatment deliveries.

In modern radiotherapy large amounts of information are available from different sources such as radiotherapy planning CT, diagnostic CT, MR, PET or SPECT, and images acquired during and sometimes after treatment providing information on inter-fraction changes. Imaging modalities like 4D CT intrinsically come with temporal information, providing information on intra-treatment changes. The image data acquired over time is in itself a source of temporal information with the potential of quantifying and monitoring treatment progress and outcomes. The increased imaging capability and computational power in recent years have also led to a blurring of the two radiotherapy phases where treatments are modified or adapted as information acquired during treatment becomes available. This paradigm shift is often referred to as adaptive radiotherapy or Image Guided Radiotherapy (IGRT).

Patient Information/Education

The internal anatomical conditions of the patient should be as close as possible to the conditions in which the CT scan was acquired. Consider e.g. the case of a prostate cancer patient; the bladder and rectum conditions should be reproduced. For the bladder, the full bladder condition, achieved by drinking a given amount of water at given times prior to each treatment fraction, is the most suitable for treatment by external beam radiotherapy and it is also reproducible with acceptable accuracy. For the rectum, the empty condition, achieved by enema, is the most suitable and reproducible in most cases. Before starting treatment a radiotherapy practitioner informs the patient about its treatment, including the importance of reproducing at treatment time the planning scan anatomical position and internal physiological conditions, e.g. bladder filling or rectum evacuation. The patient is given instructions to follow in preparation for treatment. Patient information/education is routinely delivered using drawings of the relevant internal anatomy and the way changes of anatomical conditions can affect the treatment outcome producing unwanted, often severe, side effects, and reducing treatment effectiveness (Bolderston, 2008).

1.2 Augmented Reality Potential Benefits to Radiotherapy

Advanced 3D visualization could be beneficial at several points in the RT treatment workflow. Commercial radiotherapy software uses the WIMP interaction paradigm. Although this paradigm works well with workspaces that are intrinsically 2D (word processing, publishing, image processing, etc.), it can be counterintuitive when 3D data are treated using 2D operations and views. Potential benefits of complementing, or even replacing, the WIMP paradigm with AR interfaces have been reported in the medical literature. AR has also the advantage of user interfaces being more user-friendly and intuitive, and often requiring little learning for the user, as compared to WIMP interfaces.

Accurate and intuitive visualization of complex 3D data structures (treatment volumes, organs at risk, dose distribution, CT data) is essential to the planning phase. Innovative visualization technologies have the potential to complement, improve, or radically change procedures at this stage, generating benefits to plan production, optimization, and evaluation.

Patient position verification at treatment time can involve the acquisition of an "online" CBCT scan of the patient in treatment position on the treatment couch. This procedure also involves visualization of complex 3D data; the application of novel, user friendly, and intuitive visualization techniques could be beneficial at this stage too.

User-friendly 3D visualization technology has a natural field of application to education. Patient information (that includes some form of education about internal anatomy and treatment delivery, and training to follow correct preparation and behaviour during treatment) could benefit from advanced visualization technology.

A number of Augmented Reality tools for radiotherapy have been explored and results published in a literature review ((F. Cosentino, John, & Vaarkamp, 2014), expanded and updated to the time of writing, included in this thesis as Chapter 2). In the literature review we found that:

- There are no studies based on consumer electronics devices; all studies were based on highly specialised or very expensive hardware.
- Accuracy and precision (see section 4.1 for the definition of *accuracy* and *precision*) of registration, and geometric fidelity of AR content representation, considered in studies based on consumer electronics, carried out in other fields, possibly relevant to radiotherapy, have reached levels almost appropriate to application in radiotherapy.
- Investigation of applications of AR to planning, treatment delivery, and patient education using a single coherent framework is not reported in the literature.

Considering investments made by market leader companies (Microsoft, Apple, Google, Facebook, Amazon, etc. ("Apple, Google, Facebook, and Microsoft Need Augmented Reality Coders," 2018)("How Apple leapt ahead," 2018)) AR will most likely change the way users interact with computing devices. Subsequently, the accuracy and precision of registration and the geometric fidelity of AR content representation for consumer electronics will increase in the near future.

The development of a coherent AR framework has the potential to provide valuable insight on the impact of applications of AR technology to radiotherapy. To support this view we also consider two other disciplines. As with other disciplines (e.g. surgery and architecture, section 1.1.1) AR appears to have the potential to profoundly change the way also radiotherapy professionals will make use of information technology, and a preliminary investigation of that potential will benefit from the implementation of a general framework for clinical applications development applicable to treatment planning, treatment delivery, and patient education.

1.3 Research Hypothesis

Due to the wide availability and low cost of new consumer electronics hardware platforms, offering high specification optics and computational power, based on the above preliminary considerations, and the analysis of potential benefits of application of AR to radiotherapy, we formulated the following research hypothesis.

Research Hypothesis

A user friendly AR software environment for applications to radiotherapy can be developed on low cost consumers AR platforms, without compromising on accuracy, robustness, usability, and portability to future platforms, with the following potential applications:

- *visualization aid for clinicians to enable a better understanding of 3D features of radiotherapy plans;*
- *clinical tool for patients positioning and setup errors detection;*
- *educational aid tool for radiotherapy practitioners to help informing patients about their treatment, and explaining to patients the importance of following correct preparation procedures.*

1.4 Contributions

To investigate the hypothesis we have created RAD-AR (RADiotherapy - Augmented Reality), an AR software framework for radiotherapy AR applications development. We developed three tools based on RAD-AR, to assist the radiotherapy practitioner with patient setup for treatment delivery, treatment plan evaluation, and information of patients in preparation to treatment. The tools allow the user to view the real world scene combined with computer graphics content relevant to radiotherapy, such as planning image data, any defined outlines of organs, treatment beams, and aspects of the planned dose distribution. The software's features are described in Chapter 3.

The development of RAD-AR was initially based on widely available hand held consumer tablet devices. Near the final stage of the research period of this PhD project, the state of the art AR head mounted display Microsoft HoloLens has become available in its developer version. Having planned the development of RAD-AR with portability as one of the main specifications, we have then been able to deploy RAD-AR to the HoloLens. We have carried out the following experimental studies:

- *Clinical tool for patient positioning and setup errors detection: quantitative experiments to estimate precision, accuracy, and fidelity of AR content reproduction, carried out with the RANDO anthropomorphic mannequin (Imaging Solutions, AU);*
- *Visualization aid for clinicians and radiotherapy planners: evaluation based on a user feedback study with clinicians and radiotherapy planners;*
- *Educational aid tool for radiotherapy practitioner: evaluation based on a user feedback study with clinicians and radiographers.*

The three types of applications considered above require different degrees of precision and accuracy of virtual content registration and fidelity of reproduction, as shown in Table 1.

Table 1: High Level Summary of Radiotherapy Application Requirements

	Required accuracy/precision	Required fidelity of virtual content reproduction
Patient setup	High	High
Plan visualization	Irrelevant	High
Educational tool	Irrelevant	Low

After an investigation of the accuracy of self-tracking and fidelity of virtual content rendering, and a preliminary user experience we tested the patient setup tool (requiring high accuracy, precision, and fidelity of content reproduction) for both:

- the iPad, based on the fact that better results were obtained for accuracy, precision, and fidelity of content reproduction on the iPad
- the HoloLens, considering the fact that the HoloLens delivers a more natural user experience, and expecting future improvements of the device's accuracy, precision, and fidelity content reproduction.

Preliminary experience and feedback from radiotherapy practitioners suggested a much more natural interaction of non IT specialist users with AR implemented on the HoloLens compared to the iPad; based on that, and considering that lower accuracy and precision is required for educational and plan evaluation purposes, we tested the education tool and the plan visualization tool for the HoloLens platform only.

1.5 Publications Resulting from this Research

Preliminary results of our research were published in three works.

1. Cosentino, F., John, N. W., & Vaarkamp, J. (2014). An overview of augmented and virtual reality applications in radiotherapy and future developments enabled by modern tablet devices. Journal of Radiotherapy in Practice, 13(03), 350-364

A comprehensive investigation of published works on the use of AR in Radiotherapy was carried out in 2013. A literature research was performed on Web of Science ("Web of Science") and PubMed ("PubMed"); the following keyword combinations were searched: "Augmented Reality", "Radiotherapy", "Medical Imaging", "Virtual Reality", "Image Guided Surgery". We selected for review

- all the publications dealing with applications of AR in Radiotherapy
- all the publications reporting applications of AR and VR to other field of medicine showing potential translation to Radiotherapy.

The opportunity to investigate the use consumer electronics as IT hardware base for applications of AR to Radiotherapy was pointed out in the conclusions of the paper.

2. Cosentino, F., Vaarkamp, J., & John, N. W. (2016). An Augmented Reality Tool to aid Radiotherapy Set Up implemented on a Tablet Device. In Proceedings of

International Conference on the use of Computers in Radiation Therapy. International Conference on the use of Computers in Radiation Therapy

A prototype of the system based on the iPad platform only was presented at the ICCR2016 conference (18th International Conference on the use of Computers in Radiation Therapy, 2016, London, UK, (Cosentino, Vaarkamp, & John, 2016)). Deployment to the HoloLens was included in future developments and was implemented when the device became available to the School of Computer Science of Chester University (from January 2017).

3. Cosentino, F., John, N. W., & Vaarkamp, J. (2017). RAD-AR: RADiotherapy - Augmented Reality. In Cyberworlds (CW), 2017 International Conference on. pp. 226-228.

The system was implemented on the HoloLens and demonstrated at a scientific conference (CYBERWORLDS 2017, Chester, UK, poster paper), and received the best poster award, voted by the conference delegates (Cosentino, John, & Vaarkamp, 2017).

Chapter 2. Literature Review

2.1 Introduction

In this chapter, we present a review of AR and VR applications in radiotherapy reported in the scientific literature. VR applications are considered because the conceptual framework is very close to that of AR. Also reviewed are AR and VR developments outside the radiotherapy domain where there appears to be a potential application in radiotherapy.

2.2 Treatment Planning

In radiotherapy, the first use of a stereoscopic display was reported in 1997 (Moore, Hubbold, & Hancock, 1997); an autostereoscopic display was coupled to a direct volume rendering algorithm. Two sets of preliminary experiments investigated whether subjects could achieve better depth judgements with stereoscopic images than with monoscopic ones and to explore the discomfort caused by aliasing with low-resolution images. Aliasing is a mathematical effect of signal sampling and reconstruction, leading to the appearance of artefacts on digital images reconstructed from under-sampled images. With 2D images the only effect of aliasing is the presence of artefacts, but with stereoscopic images, aliasing artefacts can be present only in one of the two views that have to be combined to give the perception of depth and this can result in user discomfort. The authors classify their results as preliminary, but observe that the results do demonstrate an overall advantage of stereoscopic over monoscopic viewing of transparent images generated by direct volume rendering. The investigation of the technique applied to radiotherapy data shows an observable improvement in the sense of depth to the image. Their results also showed stereo visualisation to have no benefit in a number of cases. The authors state that there is nothing in the way the visualisation was implemented that clearly explained this. They postulate that some subtle differences in shading on the surfaces may be more important than the stereoscopic disparities in the difficult cases. Judging from the comfort ratings, the results agree with evidence from other studies that effects of spatial aliasing may be to some extent ignored by users when interpreting stereo images.

Use of an autostereoscopic display for robotic radiosurgery planning was described in (Schlaefer, Blanck, & Schweikard, 2005). An autostereoscopic display (SeeReal Technologies GmbH, Dresden, Germany) was used. The two different views of the scene required for stereoscopic viewing were vertically interlaced in the 2D display. In order to generate the user's 3D perception a mask of beam splitters are superimposed onto the display, allowing for two different views from two different positions each corresponding to the observers left and right eyes. Treatment plans for robotic radiosurgery consist of a large number of beams directed towards the target volume. Software to visualise the resulting 3D dose distribution and the beam directions was implemented using the Visualization Toolkit (VTK) (Schroeder, Martin, & Lorensen, 2006). A hypsometric colour scheme was used to identify hot and cold spots in the target volume (i.e. regions of high and low dose, respectively). An existing treatment plan with 1,200 beams for an intracranial tumour was projected onto the autostereoscopic display to assess the spatial extent of hot and cold regions along with the orientation of the beams. Based on the visual information obtained from the 3D visualisation, 20 beams were manually added to the existing plan in such a way that a large number of cold voxels were hit, but hot voxels were avoided, helping to reduce dose to hot spots and increase dose to cold spots. An inverse planning algorithm was implemented to re-optimise the plan and the result was compared with the original plan. The original plan consisted of 119 weighted beams with a total of 21,763.3 MU (a monitor unit - MU - is a measure of machine output from a clinical accelerator for radiation therapy (Khan, 2014)). The re-optimised plan, obtained after adding 20 beams and optimised to discard the less efficient beams, consisted of 123 beams requiring 21,610.7 MU. The manually added beams were all retained with maximum weight by the optimizer algorithm. It was concluded that the visualisation tool was useful to guide optimal beam placement.

An immersive VR simulation environment RTStar (Vertual Ltd., Hull, UK), complemented with software enhancing the visualisation and simulation by using 3D stereoscopic data projection and geometric volume analysis, showed benefits to optimise beam orientations for axial 7-field IMRT plan for prostate cancer treatment plans (Shang et al., 2006). For eight existing prostate IMRT plans the beam geometry was further improved. In the 3D environment most beam angles were modified achieving a better dose homogeneity in the target area (1.9% reduction in global maximal dose). Also rectal and bladder doses were reduced (2.3% and 12.9% reduction in maximum dose, respectively). The authors also emphasised that the 3D stereoscopic viewing eliminated the risk of designing a plan that could not be delivered because of a gantry collision with the patient.

The first system to integrate volumetric 3D visualisation with treatment planning in a true 3D planning system was described in three presentations (Chu et al., 2006)(Chu et al., 2007)(Magjarevic et al., 2007). The system combined two commercially available components: the Perspecta Volumetric display System (Actuality Systems, Bedford, MA, USA) and the Philips Pinnacle3 Treatment Planning System (Philips Medical Systems, Madison, WI, USA). The Perspecta volumetric display (Figure 5) works by projecting a sequence of 2D images onto a swiftly rotating omnidirectional diffuser screen enclosed in a polycarbonate resin dome.

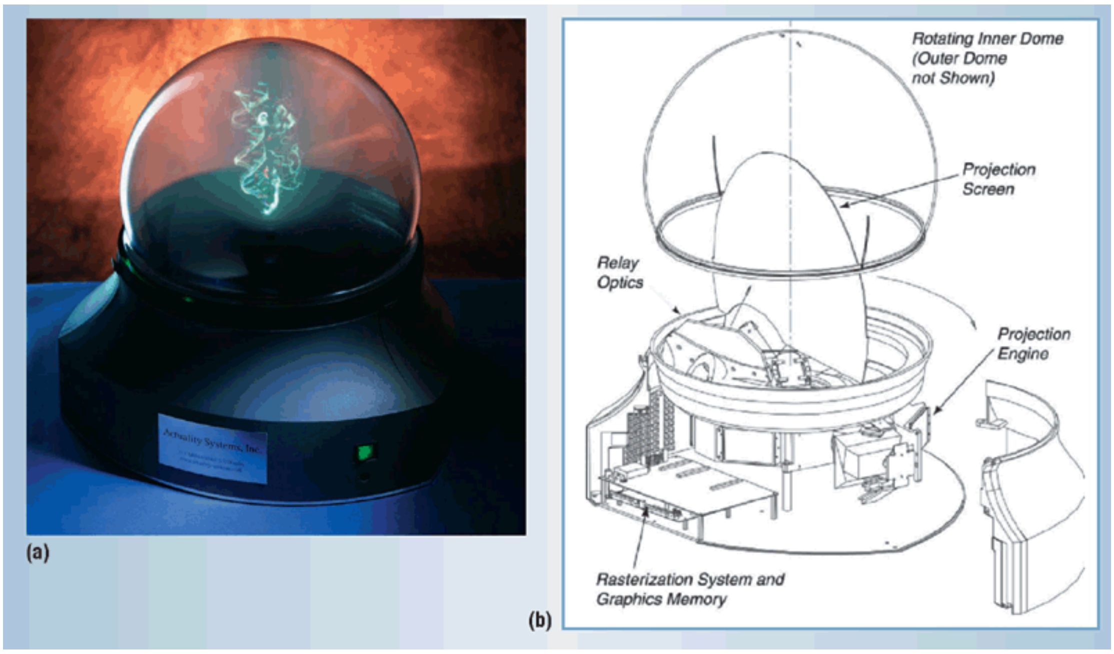


Figure 5 The Perspecta System volumetric display (from (Magjarevic et al., 2007)**).**

The treatment plans could be easily transferred between Pinnacle and Perspecta, using Perspecta for display and modification while using Pinnacle for dose calculations. To assist the radiation oncologist during the review of treatment plans, the calculated dose distribution could be rendered (Figure 5) in a volumetric 3D display (Figure 5) where anatomical information is visible in a more natural and efficient way than on 2D monitor screens.

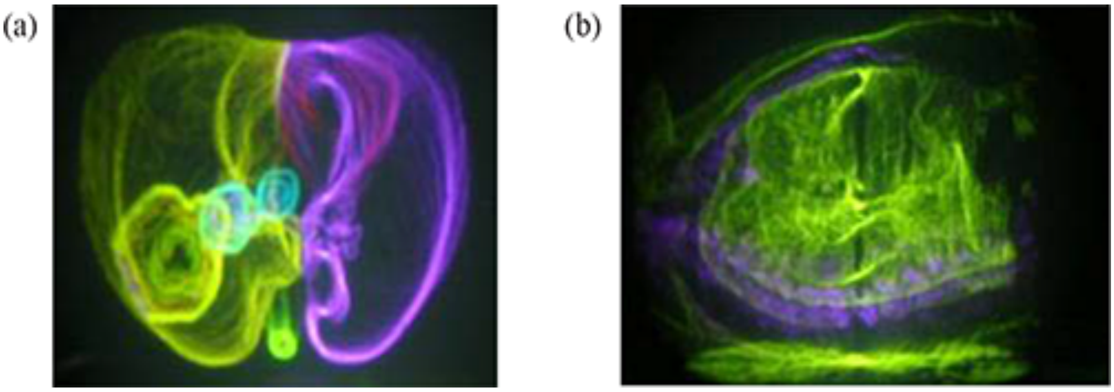
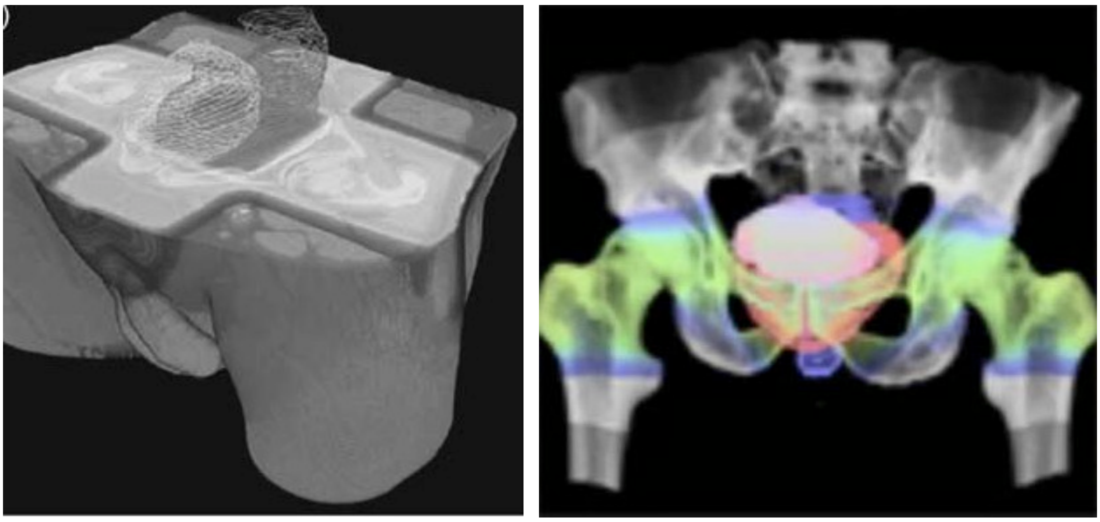


Figure 6 Perspecta autostereoscopic display of images transferred from Pinnacle planning system (from (Magjarevic et al., 2007)**). (a) Region of interest (ROI) based image. Individual ROIs can be tagged with different colours. Right and left lungs are in green and purple respectively. Tumour is bright green in right lung. Nodal disease is in blue. (b) CT-based image. Different colours can be assigned to specific ranges of CT densities. Here purple is assigned to bone.**

This enables treatment planners to create complex beam arrangements faster than with 2D monitor screens. In conventional planning the planner iteratively modifies and reviews the 3D beam geometry in relation to organs at risk (OAR) and planning treatment volumes on a 2D screen with 2D image views. This requires manipulation of the 3D image with a pointing device (mouse, trackpad, trackball, etc.), however, with the Perspecta display, the planner only needs to move around the display to change their point of view.

Quality assurance of the system was considered by Gong et al. (Gong et al., 2009). Dose at sampled points were checked and found consistent with Pinnacle within 1% or 1 mm. The 3D spatial display of images, contours, and dose distributions exported from Pinnacle to Perspecta were consistent with Pinnacle display. Distances measured by the 3D ruler in Perspecta agreed with Pinnacle. A clinical evaluation was reported in 2009 (Gong et al., 2009) with data from 46 patients: 12 brain, 10 lung, and 11 abdomen/pelvis cases, together with 13 patients from a pilot study. Perspecta plans were considered better in terms of reduced dose to OAR in 28 patients (61%). Lower doses were delivered to critical organs: 34% to the optical chiasm, 17% to the bladder, 10% to the liver, 30% to the kidney and 40% to the lungs. Surprisingly, in 14 patients (30%) Perspecta plans were worse than corresponding plans produced on a conventional planning system, and equivalent in four patients. This was attributed to volumetric 3D planning tools not yet being fully developed and the treatment planners not as familiar with the operation of the Perspecta 3D system as with the conventional planning system. The observation of unfamiliarity with the system does emphasise the need for intuitive user interfaces to effectively process and absorb large amounts of data. Despite this it was claimed that oncologist's evaluation of plans using 3D visualisation was more efficient than using 2D visualisation, because all plan information (target coverage, normal tissue sparing and the locations of hot or cold spots) from all CT slices were available simultaneously. Acceptance and quality assurance aspects and the accuracy and consistency of presenting dose information on Perspecta were also considered. It was suggested that the Perspecta display software (PerspectaRad) could be improved with the ability to commission the display to the user's specific treatment machine to include treatment machine limits.

A VR system for the evaluation of treatment plans was developed by Patel et al. (Patel et al., 2007). This was installed and networked in a radiotherapy conference room at the Haukeland University Hospital. Data were exported from the planning system and fed into the VR application for visualisation. The VR environment consisted of a passive stereo setup made by a semi-rigid back projection screen (BARCO Pas-Cad) and two overlapping LCD projectors (BARCO SXGA 3000 ANSI). Selective views for the right and the left eye were implemented by using circular polarisation filters on the projectors and matched in the user's glasses. The software ran on an up-gradable, low cost and powerful PC graphics system. By using a 2D transfer function CT and dose data were combined, where the dose at the surface of outlined or segmented structures could be rendered with good quality graphical results (Figure 7).



(a) **(b)**

Figure 7 (a) Visualisation of the dose distribution on the surface of a selected CT data volume is achieved by making all but the lowest values of the transfer function opaque. (b) Visualisation of the dose distribution on the bony structures is achieved by making areas of high CT values opaque and areas of low CT values transparent (from (Patel et al., 2007)**).**

In their paper on the clinical evaluation, the authors concluded that the adopted hardware solution was well suited for collaborative multi-disciplinary team sessions. Users can both see each other and the data simultaneously and the degree of nausea that may appear when working in VR is either absent or tolerated by the user with little or no effort. The system also provides the opportunity to inform patients about the procedure they are going through in a more informed way than traditional verbal explanations. Since the framework this system is built on already supports tracking, the authors point out it is only a question of availability of resources to be able to have it working in a completely immersed environment. The authors state that a user study quantifying the hypothesised advantage of VR (compared with the existing planning software) would be needed to further explore the potential of this software.

Butler et al. (Butler et al., 2008) investigated the impact on radiation oncologists' decision making from presenting information in 2D, 3D and stereoscopic visualisation. Stereoscopic visualisation was implemented on an Apple workstation (8 core 2.8 GHZ processors, 16 GB RAM, NVIDIA Quadro FX 5600 1.5 GB stereo 3D dual link DVI graphics card) and a 24-inch stereoscopic monitor (Planar Systems Inc.) using Osiris software. Plans for ten patients with head and neck carcinoma generated on Pinnacle (Philips) and TomoTherapy (TomoTherapy Inc.) planning systems were evaluated in 2D, 3D and stereoscopic visualisation by three radiation oncologists. The clinicians were asked if the decision-making process was changed as the display progressed from 2D, to 3D, to stereoscopic visualisation. The information provided by stereoscopic visualisation of the relationship of the target to the normal structures, with visualisation of isodose curves with depth perception, was considered clinically significant by the radiation oncologists in all ten cases. Stereoscopic visualisation did not result in changing the dose constraints for any of the plans, although the 3D display provided added assurance that the plans were safe and clinically acceptable. The authors report that in their department head and neck cancer cases are now routinely reviewed with stereoscopic visualisation.

2.3 Treatment Delivery

Deutschmann et al. (Deutschmann et al., 2008) developed a system that enables an overlay of inner structures delineated on CT data (target volumes and OAR) and field boundaries on the X-ray plane on fluoroscopy images in real time, i.e. while fluoroscopy is performed (Figure 8).

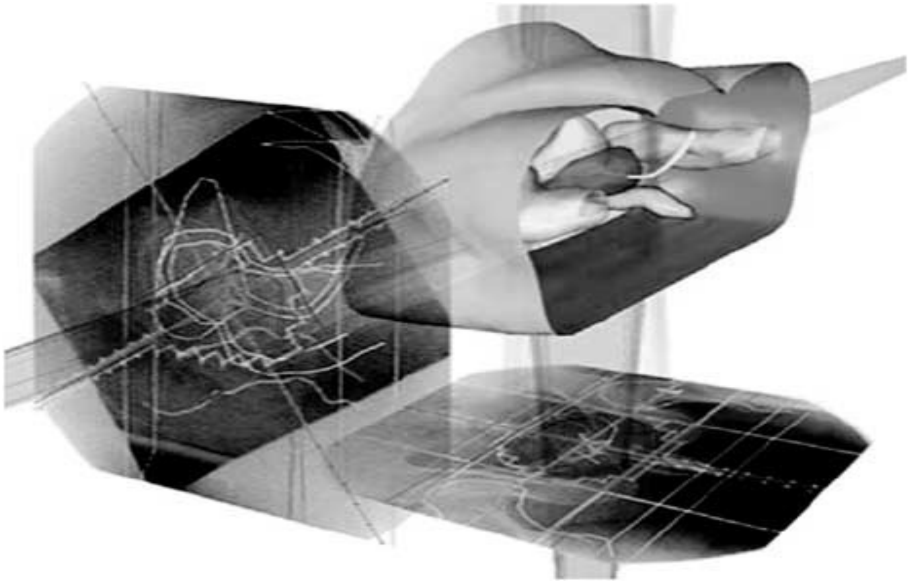


Figure 8 Fluoroscopy images matched to projection of outlined structures (from (Deutschmann et al., 2008)**).**

The simultaneous display of computer graphics imagery and real material is used to correct patient's positioning errors. More precisely, a projection onto the current X-ray image of 3-D structures not visible in the fluoroscopy because of missing soft-tissue contrast is implemented. Setup deviations between volumetric imaging and simulation were considered for 701 patients. The results of patient position adjustments based on the overlay of CT data and fluoroscopy images were superior to the results based on conventional registration of Digitally Reconstructed Radiographs and Electronic Portal Images. Applying the fast planar imaging technique and 2D-3D registration, translation errors could be corrected. A fast way to easily track rotations on planar images is still to be found.

A method for AR-facilitated patient set-up was proposed by Talbot et al. (Talbot, Meyer, Watts, & Grasset, 2009) in a pilot study using an anthropomorphic phantom. The 3D external body contour was obtained from planning CT data. With the phantom positioned on the treatment couch, the 3D body contour from planning

CT was superimposed onto a real-time video image of the phantom, using AR tracking software (Figure 9).

Figure 9 Body contour from CT scan (grey) and patient's (anthropomorphic radiotherapy phantom, red) true image (from (Talbot et al., 2009))

An operator could view the monitor placed outside the treatment room and visually confirm correct positioning throughout set-up and treatment. The performance of the system was investigated by using it to position an anthropomorphic phantom without the aid of additional set-up methods. The translational set-up errors were < 2.4 mm and the rotational errors < 0.3°. These results demonstrated the feasibility of using AR for patient positioning. The authors state that the developed technique needs further investigation before clinical use.

This approach was further investigated in (Chyou & Meyer, 2012). The RANDO phantom was used. A method based on structured light projection and detection on the patient (RANDO) body surface was used to acquire a 3D model of the patient's body shape and position immediately prior to treatment.

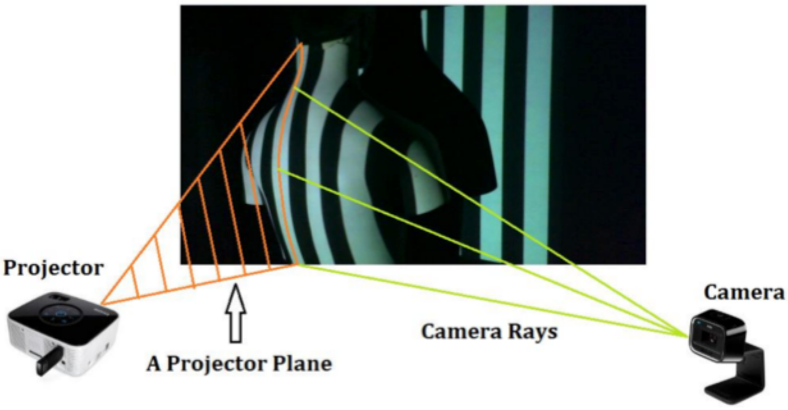
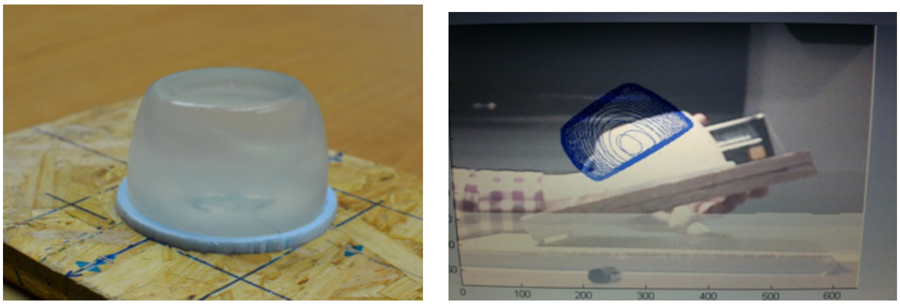


Figure 10 Relationship between a projector plane and camera rays. Each stripe projected onto body is a 3D plane intersecting with the body. When a camera sees the illuminated stripe, the position of each of the illuminated pixels on the image plane relative to the focal point defines the camera rays which form the camera image of the stripe (from (Chyou & Meyer, 2012)**).**

The two body outline models (the one extracted from the planning CT scan and the one acquired with the structured light technique) were registered (Figure 10).

Uncertainty in patient positioning was ±1 mm, ±1.5 mm, and ±4 mm in x, y, and z-directions (z is the camera optical axis).

A system built from easily sourced components is presented in (French, 2014). The feasibility of using an augmented reality 2D display as an aid for patient positioning is investigated by projecting 3D CT patient data into a live–video image of a radiation treatment suite. The virtual patient (a deformable breast phantom) appears in the planned location relative to the machine couch. The radiation therapist sets the phantom's position based on visual cues by comparison of the CT projection to the live view. The system performance was evaluated in the case of a longitudinal rotation. The positioning angles using the tool were in good agreement with the original CT angles. Angles were recovered to within 1° in most cases. In the region corresponding to the clinical data good positioning was observed to within 1.4°.



(a) (b)

Figure 11 (a) Gelatin-based deformable phantom mounted to the hinged assembly. (b) The phantom with its CT scan at an arbitrary angle projected onto the video. The user rotates the phantom assembly to match the AR image (from (French, 2014)).

True 3D display of delivered dose was investigated by Santhanam et al. (Santhanam et al., 2008). They presented a visualisation framework that combines a computer-based simulation of real-time lung tumour breathing motion and dose accumulation with an AR display system (Figure 12).

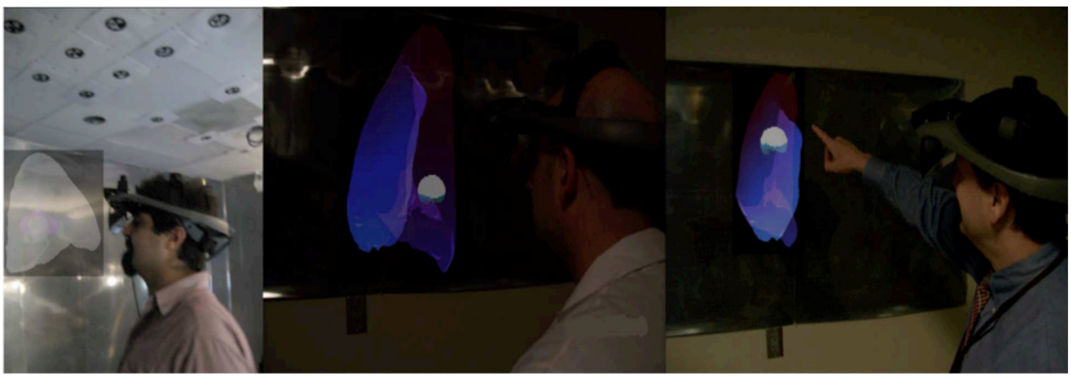


Figure 12 Real-time lung tumour motion (due to breathing) and dose accumulation, displayed on AR active glasses display system (from (Santhanam et al., 2008)**).**

The simulation framework provides visual insights on the variations in the quality of therapy for changes in the patient's breathing conditions from the pattern acquired with the 4D planning CT scan. The display system enhances the clinician's understanding by adding a 3D depth perception of the dose accumulation pattern. The framework is a tool for presenting both preoperative studies and intra-operative treatment efficacy analysis when coupled with a real-time respiration monitor. Evaluation was carried out using six clinical experts and results showed that, using AR compared with a 2D monitor, the experts were more able to efficiently perceive the radiation dose delivered to various aspects of the moving tumour and the surrounding normal tissues. Also, a quicker detection of radiation hot spots that are critical to minimising damage to healthy tissue was observed.

Wang et al. (Wang, Lee, & Fang, 2009) developed a volume visualisation system with AR interaction, using the Insight Segmentation and Registration Toolkit ("ITK - Segmentation & Registration Toolkit") and the VTK (Schroeder et al., 2006). Surface comparisons between clinically relevant isodose levels and planning volumes can give more information than conventional dose-volume histograms. A radiotherapy plan for a brain tumour was used to evaluate the software. The authors concluded that the volume visualisation with AR interaction helped the radiation oncologists to observe the under-dosing or over-dosing regions in 3D and to gain insight into the degree of dose inhomogeneity, such as hot or cold spots seen in radiotherapy plans.

A target visualisation system for real-time target verification was reported by Chen et al. (Y. Chen, Chang, Liu, & Chen, 2011). Image data from ultrasound (US) and CT scans were captured and registered. US-CT image registration was integrated with a human-commanded 6-degree-of-freedom robotic manipulation of US probe and linear accelerator to form an innovative radiotherapy system. Using an automated algorithm, target organs were segmented in CT images, US images were transformed and reconstructed to match each orientation, and image registration was performed in real-time with acceptable accuracy. This image transformation allowed oncologists to visualise CT image reconstructed targets outside BEV via an US probe positioned non-coplanar to the beams' plane. Using robotic manipulation allowed oncologists to remotely control the US probe, dynamically track and real-time monitor the coverage of target volumes within a BEV during a simulated beam-on situation. The authors concluded that their target visualisation system might provide a remotely accessible and real-time way to visualise, verify and justify the use of more conformal radiotherapy treatment technologies.

2.4 Radiotherapy Training

A notable exception where VR has taken off in radiotherapy is clinical training applications. VERT, a Virtual Environment for Radiotherapy Training (Vertual Ltd., Hull, UK, (A. W. Beavis, Page, Phillips, & Ward, 2009)(Appleyard & Coleman, 2009)(Andrew W Beavis & Ward, 2018)), was introduced into a number of English universities schools and departments in 2008, and is now installed in many other countries.

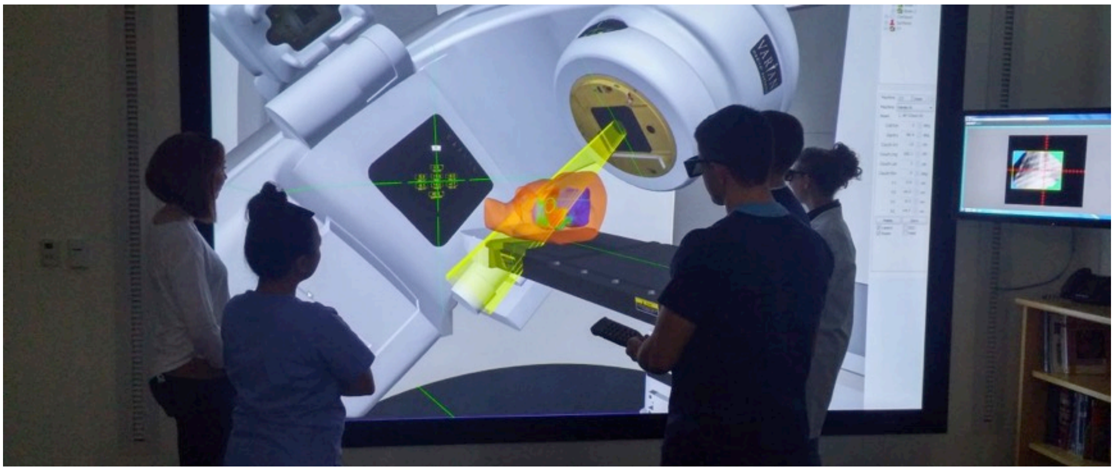


Figure 13 Students practicing in a virtual environment on a 3-D linear accelerator (from ("Radiation Therapy @ Bellevue College," 2018)**).**

The system is based on a 2D stereoscopic display (Figure 13); it allows the user to experience most procedures that can be can performed on a real LINAC, except giving a dose of ionising radiation. The user can: simulate import of patient from a treatment planning system, perform virtual patient setup with lasers/light-field/imaging, visualize CT datasets, generate imaging data and simulate an IGRT process, safely explore errors. The system can also be used in the training of physicists and dosimetrists. VERT is a specialist dedicated system, with costs in the typical region of RT specialized equipment (much higher than consumer electronics or software, typically several tens of thousands pounds with a degree of variability depending on the number of systems purchased by the institution).

A preliminary study of sickness and presence issues concluded that symptoms were minor with the most commonly reported symptoms relating to ocular issues

(Flinton & White, 2009). Subjects with a higher susceptibility to travel sickness reported disorientation and nausea, and subjects with a higher susceptibility to travel sickness showed a decrease in involvement with the VR system.

A more recent paper describes the implementation of a VERT in a radiation therapy department (Servotte, Guillaume, Boga, & Coucke, 2017). The authors state that the AR system helped to implement a standardized approach to training, with special emphasis on the definition of the training program and objectives, based on quality standards and internationally accepted terminology, and had a positive impact on building communication skills.

Use of VERT for patient information was also investigated. A pilot study (Sul e-Suso et al., 2015) was carried out in order to assess whether both patients and their relatives would benefit form further information on RT treatment using a virtual reality technology. One hundred and fifty patients were included in the study and were shown a standard room where RT is given and how RT is planned and delivered using their own planning CT Scans. Information was given on a one-to-one basis to patients and some of their relatives. Information was welcomed as it helped them to reduce patients' fears and understand more about their treatment (about 80% of patients) and relatives felt also more involved in the treatment of their loved one. The authors conclude that VR aids could become an important information tool for patients and their relatives.

Patient information with a combination of real footage and 3D visualisation software based on VERT was investigated in (Williams, Blencowe, Ind, & Willis, 2017); the authors report that the considered approach assisted in meeting learning objectives about the treatment process.

In a recent survey the future role of AR in radiation oncology education and training was considered (Jin, Birckhead, Perez, & Hoffe, 2017). A systematic review was performed, based on a literature query combining the search terms "virtual", "augmented", "reality", "medical student", and "education". The aim was to find articles that examined AR/VR surgery-naïve students learning anatomy and receiving first-time training of procedural tasks. Studies were excluded if non-stereoscopic VR was used, if they were not randomized controlled trials, or if resident-level participants were included. The authors conclude that radiation oncology has opportunities for AR/VR simulation in both training and clinical practice; for learning anatomy and procedural tasks, the studies considered suggested that AR/VR was non inferior to current standards of practice with regard to learning anatomy and training in procedural tasks, and that radiation oncology would benefit from AR/VR technologies in terms of cost-effectiveness, by enhancing training in a field with a narrow therapeutic ratio.

2.5 Consumer Electronics Devices to Interact with Clinical Data

Technology is changing at a rapid pace and some developments have the potential to profoundly change the way clinical professionals interact with computer-generated data. In particular there is a growing number of adaptations of consumer market technology (game controllers, handheld devices) as an alternative to highly specialised hardware.

Accuray PlanTouch ("Accuray Rolls Out PlanTouch," 2014) is the first commercially available software application in radiotherapy that allows oncologists to remotely review and approve radiotherapy plans on the Apple iPad. The application's interface is fully integrated with the CyberKnife planning software. Oncologists can review dose volume histograms, isodose curves, contours and images and approve treatment plans directly from their tablet devices. Treatment planning displays are designed and formatted specifically for the iPad's screen and can be manipulated using the iPad's touch screen capabilities. There are a number of other companies supplying equipment to radiotherapy clinics releasing software for users to review or approve information on handheld devices, for example clinical information that is available during ward rounds.

An example applied to brachytherapy is given by Butler (Butler, 2011). When performing a needle implant for advanced gynaecological malignancies, it is often difficult to predetermine parameters like needle length to target, proximity to bowel and vascularity. To overcome these difficulties laparoscopic guidance is often required. In this example, 3D interactive volumetric display software, utilised by other subspecialties (e.g., cardiovascular interventions), is evaluated to see if it can replace laparoscopic guidance. For a patient with a clinical condition preventing the use of laparoscopic guidance, needle placement utilising the visualisation system as guidance was evaluated. A CT angiography study was fused with a PET imaging study and used to define and refine the target. Before going to the operating room, guidance data (ideal trajectory of needles and other relevant parameters) were predetermined and recorded on an iPad. The iPad was taken into the operating room and used to display the guidance data for additional insight during the intra-operative procedure to complement fluoroscopy, the only other diagnostic imaging available in the operating room. Postoperative CT imaging verified needle placement to be within 2 mm of ideal placement. There were no operating room complications. The author concludes that 3D volumetric reconstructive software can assist the radiation oncologist in preplanning brachytherapy needle placement but, in order to optimise the 3D volumetric reconstruction process, the radiation oncologist needs to understand the geometry of the CT datasets.

Nakata et al. (Nakata et al., 2012) designed a system for 3D and 4D image manipulation using optical tracking AR integrated with a smart-phone. The authors observed that the mouse, the most widely used pointing device on personal computers, was originally designed and best suited for control of 2D cursor movement rather than complex 3D image manipulation. In this work, 3D and 4D images obtained with CT and magnetic resonance imaging were displayed on a PC running Windows 7 (Microsoft). The AR software was based on ARToolKit ("Open Source Augmented Reality SDK," n.d.). In this novel system, the authors used the iPhone or iPod Touch as a remote control device. The functions of this remote control included zooming in or out on the AR object, capturing the PC screen, and playing or pausing the 4D object, and were achieved using a Wi-Fi connection. The system allowed radiologists to browse 3D or 4D images from CT and MR imaging by using an iPhone or iPod Touch to control the PC. AR images required surface rendering, which was achieved by using OsiriX ("OsiriX," 2017) imaging software. The surface image data were transferred to a Windows PC with a novel AR viewer developed by using the ARToolKit. The PC was equipped with a web camera allowing recognition of the AR fiducial marker. The software allowed radiologists to manage the AR images using either an iPhone or a conventional two-button mouse as a controller for comparative evaluation. The iPhone or iPod Touch was placed in a plastic jacket with an optical tracking marker printed on the back. The radiologist could move and twist the iPhone or iPod Touch with the optical marker facing the web camera of the PC and the software running on the PC was able to recognise the optical marker. The AR images were shown on the LCD display of the PC with real-time tracking as a superposed model of the optical marker on the background of the real-world view as seen on the LCD monitor. When the radiologist moves the iPhone or iPod Touch, the

3D object on the LCD monitor moves and scales itself at the same time in an intuitive manner. The authors concluded that, although strict comparisons of user interface performance between the AR techniques and a conventional mouse are difficult, AR had high interactivity and 3D image manipulation required no special training. Therefore, performance evaluation of the AR technique was performed without special warm-up trials. They compared the performance of the AR 3D image manipulation method with that of the conventional method. Three different 3D objects were evaluated by 12 different testers. The times for three horizontal predetermined rotations of each 3D object were measured. The average times to perform the rotations with the AR method were statistically shorter than those achieved with the conventional two-button mouse in all three cases.

A novel user interface to provide a direct interaction with medical imaging data in 3D space by off-the-shelf input devices was proposed and evaluated in [67][68]. The interface was implemented as open-source software and integrated into the open-source medical image viewer Medical Imaging TOolkit MITO [69]. Both a common mouse and a Wii remote controller were used as input devices (Figure 13).

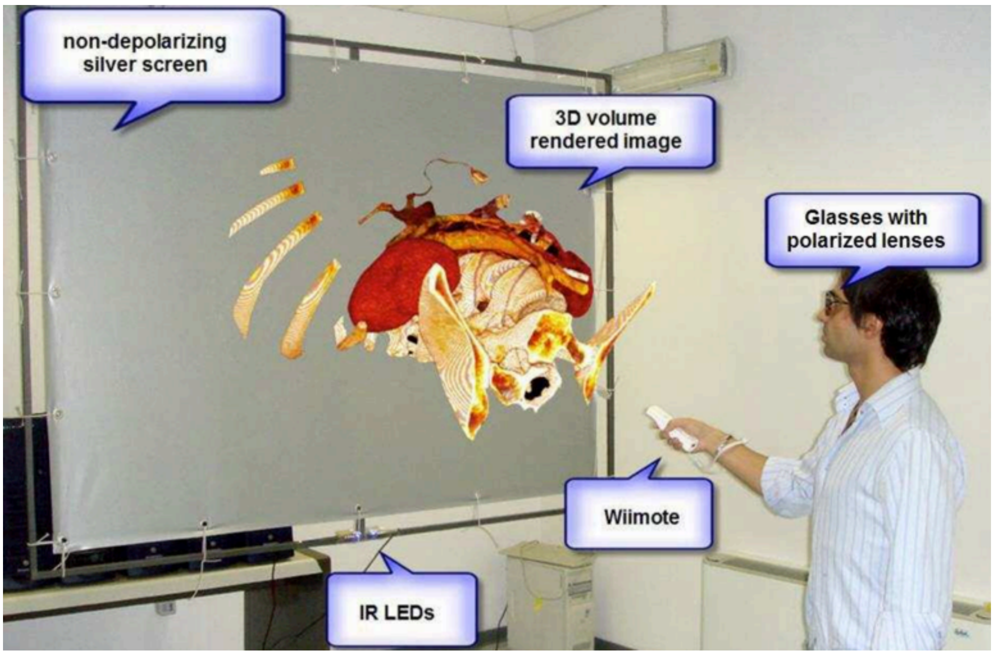


Figure 14 Direct interaction with medical imaging data in 3D space integrated into the open-source medical image viewer MITO (from [67]).

The interface featured a novel rotational technique using the geometry itself as the rotation handle. A user study showed that the proposed techniques were easy-to-learn and outperformed the virtual trackball technique in the task of rotating complex-shaped objects.

AR applications supporting innovation and accuracy in radiotherapy were studied in (Spoto, Bourhaleb, & Petrone, 2016). A tool based on AR working on tablet or smartphone was developed. Users get real-time information about any equipment in the treatment room by pointing the device at it. An AR client recognizes the medical equipment and gathers corresponding information from a cloud server. Access to the data server is secured with different level of privileges; according to their role users can only visualize and use predetermined types information. All medical information related to the patient is stored in a private cloud and needs proper authentication to be accessed. Three use cases are considered: medical doctor, medical physicists and technical engineer. The authors conclude that AR is an ideal candidate to help healthcare providers to improve precision and efficiency of existing processes. Precision is intended as providing correct end relevant information in a robust way, and in real-time, responding to the specific needs of different users, and related to systematic tasks that are daily in radiotherapy facilities to assure the quality of delivered treatments.

2.6 AR and VR Techniques in Other Domains Showing Potential Application to Radiotherapy

In this section a number of AR/VR examples in medicine, or even outside of medicine, illustrating potential applications in radiotherapy, are considered. Registration of the real world, as seen for example through a device's camera, and computer-generated imagery being merged with the scene is a far from trivial task, especially in real time. The examples in this section, however, demonstrate that this can be accomplished with error margins of the order of 2 mm or less. This spatial error margin is accepted in many radiotherapy techniques. A considerable improvement of accuracy has been achieved between the first example considered below dating back to 2002 and the more recent studies. In 2002, Mitchell et al. (Mitchell, Wilkinson, Griffiths, Linsley, & Jakubowski, 2002) described a method of image guidance for neurosurgery using the surgeon's binocular depth. For patients with brain tumours, stereoscopic pairs of images of the surface rendering of the head and the surface rendering of the tumour were produced using MRI data. The two pairs of images were colour-coded and combined into one pair of 35-mm slides viewable using an ad-hoc constructed stereoscopic viewer. Registration was achieved by moving the stereoscope in space until the virtual images of the rendered surface of the head coincided with the real head. The stereoscope was then locked in position and the virtual image of the tumour was projected inside the patient's head, allowing the surgeon to locate the tumour. Six clinical cases were considered. A lateral accuracy of 10-15 mm and a depth accuracy of 5-10 mm were achieved.

Another application of AR to conduct minimally invasive orthopaedic surgery was reported by in (Liao et al., 2010). This paper describes a precision-guided surgical navigation system, that consisted of a combination of laser guidance and 3D autostereoscopic image overlay. Using an integral videography imaging method, images of surgical anatomic structures were superimposed onto the patient without the need for special viewing or tracking devices (Figure 15).

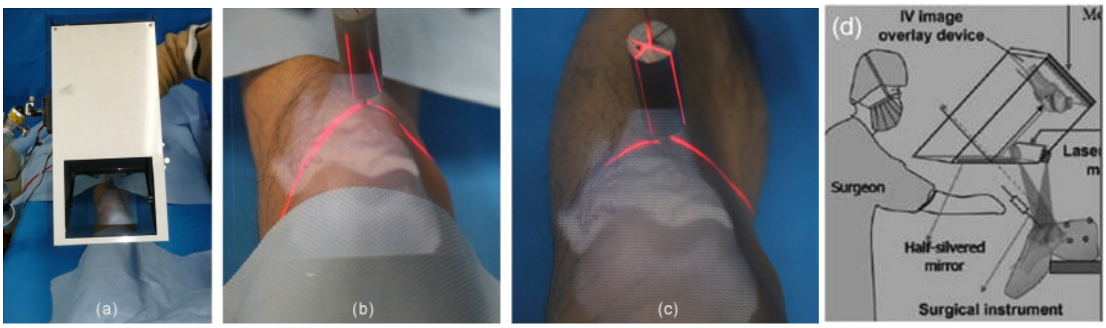


Figure 15 Laser guidance with autostereoscopic image overlay: (a) IV image overlay device and patient/image overlay; (b) alignment of surgical instrument; (c) image-patient registration results and surgical path guidance of laser beams; (d) operational diagram (from (Liao et al., 2010)**).**

The image overlay system was integrated with a laser guidance system to improve the placement accuracy of surgical instruments. Experimental evaluations showed that the error in guiding a linear surgical instrument towards a target was within 2.48 mm with a standard deviation of 1.76 mm, and the orientation error was 2.96° with 2.12° standard deviation. This is the same order of spatial accuracy required in modern external radiotherapy (International Commission on Radiation Units and Measurements, 1999). The authors concluded that the system can support surgeons during their operations and enables them to intuitively identify the insertion path of the surgical instrument. It was also stated that accuracy could be improved by using a display device with a higher pixel density and a higher precision laser guidance device. This would make the system of practical use not only for orthopaedic applications, but also in other medical fields. An application in radiotherapy for the 3D autostereoscopic image overlay systems could be displaying patient's outlined anatomy, planning volumes and planned treatment beams, in the treatment room overlaid to the patient, before treatment as a verification aid.

A VR MRI navigation system for breast-conserving surgery was developed in (Tomikawa et al., 2010). The authors report an estimate of the mismatch between VR content and real distance to be in the order of magnitude required by radiotherapy applications. Clear analogies between concepts considered in this study (image registration, surgical margins) and fundamental concepts in radiotherapy (image registration, treatment and OAR margins) suggest possible applications to radiotherapy. In this work dye marking of a breast tumour, serving as guidance for surgical resection, was performed using a real-time 3D VR navigation system. A pilot study using a 3D phantom was carried out for quantitative and qualitative evaluations and a mean mismatch between the navigation system and real distance of 2.01 ± 0.32 mm was reported. A study based on two patients was also carried out. Histopathological examinations of the resected specimens of the two patients showed that the surgical margins were free of carcinoma cells.

Kim et al. (Kim et al., 2011) developed a dual surgical navigation system for endoscopic surgery that used VR and AR techniques together to obtain additional depth and visual information for organs. The VR environment was developed to visualise the spatial relationships among the target organs, endoscope and surgical tools. The AR environment was used to display the raw endoscopic images with the nearby organ images overlaid, as obtained from CT and MRI scans, which would otherwise be invisible to the endoscopic probe. Surgeons were enabled to better understand the surgical environment around the target, increasing the safety and accuracy of surgical procedures. Image registration between endoscopic and CT/MRI data was realised using a surface-tracking technique. A virtual model of the endoscope and surgical instruments were displayed into the VR and AR environments based on tracking of the endoscope and instruments position; tracking was carried out using either an optical position sensor or an electromagnetic sensor. Raw endoscopic images are affected by distortion due to camera optics. In order to accurately overlay CT/MRI data on to endoscopic images, camera optics transformation was applied to CT/MRI images. This was realised through camera calibration procedures that allowed the relevant geometric parameters and the lens distortion coefficients to be obtained. Rendering was based on the parameters of the endoscopic camera, so the rendered results mimic the shape and size of the real object, just as it would appear from the endoscopic video camera. In phantom experiments, the translational overall registration error was < 2 mm with CT images and an optical position sensor. Higher errors were observed using an electromagnetic tracking sensor and MR images. Correlation between errors and endoscopic camera angles were also observed. The dual navigation system was applied to a cochlear implant surgery for evaluation in a clinical setting. The system was applied to a surgical microscope instead of an endoscope and the clinical application analysis confirmed the feasibility of such a system in the operating theatre. The surgeons who have observed and used the system in the clinical study declared the usefulness of the dual navigation system, considering it to have significant advantages compared with conventional systems.

Gavaghan et al. (Gavaghan et al., 2012) developed a portable image overlay projector for the visualisation of surgical navigation data and conducted some tests on phantoms to explore the capabilities of the device. Monitor-based visual feedback for image-guided surgery requires the surgeon to perform time consuming comparisons and diversion of sight and attention. Their system utilised a portable image overlay device comprising a navigation computer unit, an infrared-based optical passive tracking system (Vicra, NDI, CA, USA) and touch screens for user interaction and visual display (Figure 16).

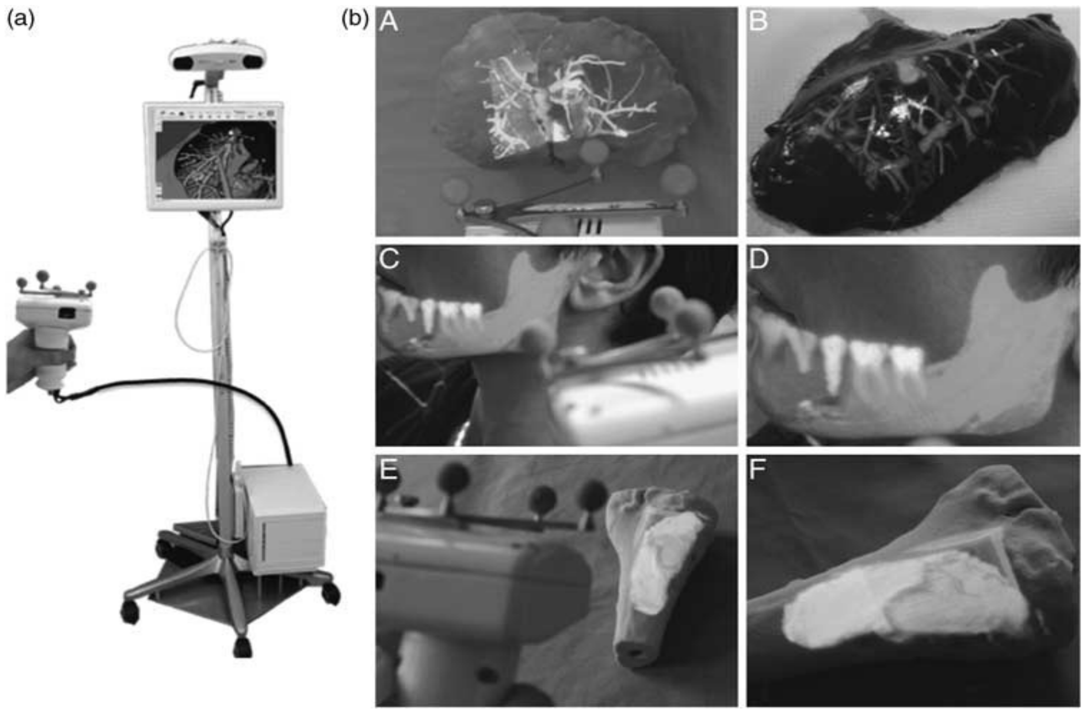


Figure 16 (a) Stereotactic instrument guidance system with integrated image overlay device. (b) (A) Image overlay AR for navigated liver surgery on a patient-specific rigid model and (B), pig liver tissue; (C, D) image overlay AR for navigated cranio-maxillo facial surgical planning; (E) and (F) image overlay AR for navigated orthopaedic tumour resection (from (Gavaghan et al., 2012)**).**

The optical cameras are able to track known configurations of retro-reflective marker spheres. The system was tested on a range of anatomical models and for planning different surgical interventions (liver, cranio-maxillofacial, orthopaedic and biopsy). The visualisation approach was found to assist in spatial understanding and reduced the need for sight diversion throughout the simulated surgical procedures. The portability of the device and intuitiveness of use suggest an expansion of its application to other parts of medicine, including radiotherapy especially for the patient positioning phase, where monitor-based systems would pose problems of portability and ease of use inside the treatment bunker.

Another study reporting an estimate of the registration accuracy between the real scene and AR content is (Low et al., 2010) where AR neurosurgical planning and navigation system (the DEX-ray) for surgical excision of meningiomas were implemented. The DEX-ray system is based on the Dextroscope (a stereoscopic 3D pre-operative planning system) and allows the transfer of the Dextroscope planning data into the operating theatre by displaying it on to real-time images, producing in this way a video-augmented presentation of the surgical scene, further enhancing the appreciation of the tumour's location in 3D space. The DEX-ray has an image distortion < 0.4 mm in the AR mode and a registration accuracy of 1-3 mm. The AR feature allows for navigation with 3D graphics beyond the visible surface of the surgical site, but yet always in direct context to it, providing a see-through effect and resulting in a more direct understanding of the hidden anatomy relevant to the surgical procedure.

Several architecture-oriented applications of AR implementing visualisation of virtual buildings overlaid on the real scene are found on the web. CityViewAR ("CityViewAR," 2015) is an AR application designed at Canterbury University, New Zealand, to give a visual reminder of how the city of Christchurch (New Zealand) used to look before the earthquake in 2010. Similar applications, but in the entertainment domain, are reported online, for example by String Labs Limited ("String"). These last two examples support the view that applications of AR to radiotherapy based on self-tracking capability of tablet devices are feasible. Moreover, for these consumer devices programming techniques are more reusable than for highly specialised devices requiring more low-level programming. This may make the required programming knowledge more readily available, although for some time yet multi-disciplinary collaboration involving specialist developers is likely to be needed to make best use of these tools. The accuracy and reliability achievable by these systems needs further investigation.

2.7 Recent Developments in Medical AR using Head Mounted Displays

A number of studies based on head-mounted displays are starting to appear in the scientific literature. Qian et al. (Qian et al., 2017) present a systematic approach to evaluate optical see-through head-mounted displays (OST-HMD) technologies for specific clinical scenarios, restricting the study to object-anchored 2D-display of medical information. The authors consider three OST-HMD: Microsoft HoloLens, ODG R-7, and Epson Moverio BT-200 and conclude that Microsoft HoloLens performs best among the three tested devices in terms of contrast perception, task load, and frame rate.

In (Adabi et al., 2017) a commercial software (HoloMeasure) for Microsoft HoloLens is used for applications in plastic surgery. Virtual lines were projected and measured between anatomical parts relevant to a surgical procedure. The same distances were also measured using a standardized ruler and the mean error of these measurements and the user variability was calculated. Users were asked to answer a survey assessing comfort level, ease of use, and overall satisfaction, graded on a five-point (1 to 5) Likert (Likert, 1932) scale. Successfully made precise measurements of breast and body parameters routinely used in plastic surgery were obtained with the AR method. The mean error of distance measurements was 4.3% with a standard deviation of 0.71 among users. The average ease of voice-activated controls was 4.5; the average ease of using the hand gesture features was 4.7. The authors conclude that the HoloLens can make accurate and reproducible measurements in plastic surgery, and that the technology is accessible and comfortable for surgeons using the device.

Mohiuddin et al. (Mohiuddin, Flynn, Buatti, & Xia, 2017) implemented a radiotherapy plan visualization tool on the HoloLens. This study demonstrates a practical method for transition from indirect 2D visualization of the planned dose distribution using isodose lines to direct 3D evaluation of isodose volumes. Findings show that the advantages of holographic visualization include rapid global assessment of large treatment fields without loss of critical spatial data (as caused by dose volume histogram based analysis). Prior treatment plans visualization as holograms is also considered, to improve understanding of cumulative irradiated volume effects.

An AR surgical holographic navigation platform based on Microsoft HoloLens for open and minimally-invasive spine surgery was recently introduced on the marked by Scopis (Scopis Medical, Berlin, Germany, ("Scopis," 2017)). The company claims that "Incorporating Microsoft HoloLens into their conventional display-based navigation platform, the new system lets surgeons plan very delicate aspects surgical procedures where the highest levels of precision and speed are critical…" e.g. "in neurosurgery, for example, brain tumours could be located faster and with higher accuracy". Accuracy of mixed reality overlay is improved using additional 3-D position tracking.

A spin-off company, HoloSurg3D (San Francisco, CA 94127, (Courtier, 2017)) released an AR software, RadHA, that allows surgeons to view radiology images on the HoloLens projecting 3D images onto a real-world background. The company claims that "This helps surgeons to better: Educate patients about their surgeries, understand complicated anatomy before surgery, 'Roadmap' important structures during surgery, making surgery faster, safer, and more efficient."

2.8 Summary and Conclusions

The review of novel systems based on AR user interfaces considered in this chapter suggests a future where radiotherapy professionals will be able to manipulate 3D and 4D images in a more intuitive and efficient way, possibly anywhere, anytime. This is likely to enable a better use of large amounts of information available with modern diagnostic tools, but more radically may change how collaborative tasks such as clinical case discussions or complex case planning can be performed. The reviewed radiotherapy studies point to potential benefits from AR at various parts of the treatment process. Most of the early studies suggest that research in this field will need to address current limitations around operator discomfort, ease of use, and sensible selection and accuracy of information to be displayed. Accuracy of the registration between virtual content and the real scene is reported to be in the order of few millimetres (or less) in recent VR/AR applications to surgery (Liao et al., 2010)(Tomikawa et al., 2010)(Kim et al., 2011)(Gavaghan et al., 2012)(Low et al., 2010), similar to the accuracy required for most advanced radiotherapy techniques

(International Commission on Radiation Units and Measurements, 1999). A reduction of the registration error from 5-10 mm to 1-2 mm has been achieved from 2002 [68] to the present date. If this trend continues the registration error will be made significantly smaller than the spatial accuracy required in radiotherapy for patient positioning and treatment planning, possibly negligible and the introduction of AR setup and verification tools in radiotherapy will be feasible in the foreseeable future.

Despite promising results, AR has not taken off in clinical radiotherapy to date, with the exception of teaching and training applications. This may be partly because of the high cost of equipment, explaining the difficulties to develop this into commercial tools. However, the situation is rapidly changing and the cost of high specifications AR and VR capable hardware is considerably decreasing. Although there was a considerable time lapse between the first (Moore et al., 1997) and the second (Schlaefer et al., 2005) study reporting 3D display applications in radiotherapy, since that time the number of publications in this field are steadily increasing, indicating a growing interest from the medical and scientific communities. The majority of the reviewed studies used costly hardware not widely available commercially, especially holographic displays and state-of-the-art large flat-screen 3D displays and projectors.

More recent studies have started to use readily available devices (Wii remote, iPad, iPhone, iPod Touch), where interestingly none of the systems based on these devices have reported problems of user discomfort, requirements of special training or cost. The use of tablet and handheld devices (e.g., iPad, iPhone, iPod Touch and Android equivalents) is growing fast and these devices are being rapidly adopted in the medical field, particularly for medical imaging applications. Most tablets also have a built in camera that can be utilised for AR applications. However, computing power on a tablet is limited and the real time registration of the camera image and computer-generated graphics remains a challenge. In summary, the development of small mass-produced tablet devices coming on the market will allow the user to interact with computer-generated information more easily, facilitating the application of AR and VR to radiotherapy practice.

From 2016 onwards, a number of head-mounted display (HMD) systems appeared on the technology market available either as a development version or as a consumer final version, or both. Medical applications of this category of devices can easily be imagined. The only applications to radiotherapy found in the literature to date are (Spoto et al., 2016), a study focussed on procedural information display as 2D AR content, and (Mohiuddin et al., 2017), a recent feasibility study of 3D radiotherapy data visualization (no experimental quantitative evaluation of the system was carried out). No direct applications of HMD to the radiotherapy treatment phase are found in the scientific literature to date. Use in medical education instead was considered among the main application fields from the beginning, as witnessed by the availability of anatomy teaching demos bundled with the developer edition of HoloLens. Some applications to medical volume data display was considered in (de Ridder, Jung, Huang, Kim, & Feng, 2015). Some HMD based commercial products (Scopis) for medical applications introduce improvement of accuracy tracking ("Scopis," 2017); other (Courtier, 2017)) claim applicability in al phases of the medical surgical procedure (planning, surgery, patient training).

Conclusions drawn in (Jin et al., 2017) suggest potential applications of AR to patient information, as the review showed positive impact on learning for students with little or no preliminary knowledge of internal anatomy, starting to learn anatomy or receiving first-time training of procedural tasks, and patients on average have little or no knowledge of internal anatomy relevant to their treatment, and this can affect negatively their ability to adhere to treatment preparation requests to maximise the effectiveness of treatment offered (Van Biesen, van der Veer, Murphey, Loblova, & Davies, 2014)(Tian, Jia, & Cheng, 2015). Benefits to patients in understanding the treatment and to their relatives feeling more involved was reported in (Sul e-Suso et al., 2015), where VR implemented on expensive specialized hardware and an expensive software was used (total cost of the system of the order of several tens of thousands pounds).

It is realistic to assume that HMDs will have the potential to play a major role in the development of medical visualization technology. Support to this statement comes also from Chen et al. (L. Chen, Day, Tang, & John, 2017) where research trends in the field of medical mixed reality have been analysed with unbiased and fully automated data mining techniques. A large corpus of research papers, based on the Scopus literature database, where selected (1,403 publications) analysed. The authors conclude that the feasibility of mixed reality systems for medical applications has been demonstrated by an ever-increasing number of research projects. A number of technical challenges are identified (real time performance with high precision and minimum latency, accuracy of tracking and registration, accuracy of patient specific data modelling), and often the reluctance of the medical profession to embrace changes in their field is also seen by the authors as a cultural challenge, but the conclusion is that that the medical domain is on the cusp of adopting mixed reality technologies into everyday practice. We share that view and we believe that AR will significantly change how radiotherapy professionals will work, to the benefit of patients.

Chapter 3. RAD-AR Software Development

3.1 RAD-AR Development: Specification of Software Functionalities

To investigate the research hypothesis of this thesis (see section 1.3) we have developed RAD-AR (RADiotherapy - Augmented Reality), an AR framework for radiotherapy applications development. RAD-AR allows development of applications on AR ready consumer devices, where the user is able to view the real world scene combined with computer graphics content representing aspects of a radiotherapy treatment anchored to the real world scene. All the software functionalities within RAD-AR are formulated to allow portability to the main AR hardware platforms. Functionality requirements also come from the experience of working in a cancer treatment department of a major regional hospital, the North Wales Cancer Treatment Center (NWCTC, Bodelwyddan, UK), and through discussions with practitioners.

To define the main characteristics of RAD-AR we focussed on a particular aspect of AR that can produce benefits in radiotherapy: the capability to make visible some of the main aspects of a radiotherapy treatment that are not directly visible. These can be divided in two categories:

- elements that are physically existent in 3D space but are invisible to the naked eye, such as radiation treatment beams, and can only be detected by physics instruments
- purely virtual objects that have a direct 3D spatial interpretation, like treatment volumes outlines, organs at risk outlines, isodose surfaces, etc.

Both categories are represented as virtual 3D content that can be overlaid to the real scene view and statically anchored to a physical location in space. Allowing the user to choose the visual characteristics of the virtual content is essential, as the optimal choice in terms of user perception of transparency levels, colours and rendered materials depends on several factors such as user subjective preferences, real scene properties (illumination, complexity of the background, etc.) and features of the radiotherapy treatment that are of interest in a specific context. User selectable graphical properties allow a better understanding and perception of the treatment aspects of interest in different conditions. Software functionality (I) was then defined as:

(I) Virtual 3D content is displayed anchored to the view of the real world, with user selectable transparency, rendering, and colour effects.

For the system to be suitable for use in a radiotherapy clinical setting we make a requirement (II) on registration accuracy:

(II) Accuracy of registration of virtual content with the view of the real world has to be of magnitude similar to precision required in radiotherapy treatments.

To allow the user, depending on the situation, to either focus on a particular aspect or have a comprehensive understanding of the treatment, we included functionality (III):

(III) The visualization of each virtual object can be switched on and off by the user.

We also wanted to display CT scan data, as they represent crucial information in a radiotherapy plan. There were two options: volume rendering (which includes ray casting and surface extraction techniques) and single CT slice rendering. In regards to the benefits of CT slice rendering, we speculated that navigation of CT slices anchored to the physical word would have added geometric and spatial insight to the conventional 2D display slice visualization. Hence, we included functionality (IV):

(IV) Single CT slices are rendered anchored to the physical world with the possibility given to the user of navigating through CT slices.

Due to portability and computational requirements, volume rendering was discarded (although a similar effect based on a simpler technique will be considered) because this is an open research problem for most AR systems ("BaAr Hololens,"

2017) and would constitute a major research topic in itself. Although true volume rendering was discarded, we were interested in a preliminary investigation of the benefits produced by semi-transparent visualization of volume CT data. In order to consider this aspect functionality (V) was added:

> *(V) subsets of the CT dataset, with position and thickness selected by the user, are rendered with a suitable degree of transparency to produce a pseudo volume rendering visualization.*

To implement (V) a simple solution simulating slice based volume rendering (Kruger & Westermann, 2003)(Swan & Yagel, 1993), technically feasible with reasonable effort, was adopted.

Functionalities (I) to (V) considered above raise no issues of portability between different platforms (e.g. tablets, AR visors, etc.). A more uncertain point was instead the choice of the functionalities for the user control interface as it would appear in the augmented reality scene. We needed toggle switches, for example to switch on/off the display of different virtual objects, multiple choice switches to allow the user to change material rendering, slider bars to change virtual content position, orientation, and dimensions, and to navigate through CT slices. Such controls are directly supported on tablet platforms but are not available as off-the-shelf assets for most AR visors, and when available, they don't always work properly on the HoloLens ("Slider working in Unity but not in Hololens," 2017). A rudimentary version of this class of controls available in the HoloLens SDK is inherited from Unity but in order to keep the software portable to other holographic visors, an alternative approach was to build control switches and sliders as 3D virtual objects with constrained motion, either along a straight line (sliders) or between two or more fixed positions (switches), with their position controllable by the user. The position of the controller objects are linked to, and control, the aspects of the parameter that we want to control on the radiotherapy AR objects. The aesthetics of the resulting user interface is not very refined but the main criteria for this thesis was to provide the functionality needed and the aesthetics of the user interface had low priority. If aesthetics of the user interface is important and the application does not require highly specialized or customized user interaction, the basic UI controls provided by Unity are adequate.

3.2 Rationale for Development Strategy and Selection of Development Frameworks

Based on the published literature review, cost aspects, hardware quality, and specifications and software robustness requirements, the initial choice of the development platform for RAD-AR was iOS. An initial assessment of available software libraries was then carried out. The number of AR frameworks available was relatively large; more than 25 different libraries covering a variety of operating systems were cited on a comparison web site (“Augmented Reality SDK Comparison,” 2015). The same web site includes today more than 70 frameworks, 40 of which supporting iOS.

Restricting the field initially to iOS (see section 3.3) and considering licensing issues, we considered the following AR frameworks: Metaio (“Metaio”), ARToolKit (“Open Source Augmented Reality SDK”), Vuforia (“Vuforia"), CraftAR (“Catchoom Craftar,” 2018), and when it became available, the Microsoft HoloLens SDK for Windows 10. A preliminary experimental investigation of camera pose accuracy was performed (the same procedure described in section 4.2 but with a smaller number of measurements – about 40 samples for each SDK) for the iOS implementation. For ARToolKit we found that errors were of the order of 4 mm to 25 mm for (our findings are consistent with literature (Malbezin, Piekarski, & Thomas, 2002)(Abawi, Bienwald, & Dorner, 2004)). For CraftAR errors were of the order of 8 mm to 20 mm. Preliminary investigation of Vuforia and Metaio resulted in an estimated accuracy of 1 mm to 5 mm, consistent with results reported in literature (Kiss, Palmer, & Torp, 2015)(Pentenrieder & Platonov, 2006). ARToolKit and CraftAR were discarded for both accuracy and ease of use issues, especially when compared to Metaio and Vuforia.

The development environments considered were Apple Xcode (“Xcode”), Apple Swift (“Swift”), and Unity (“Unity”). The earlier aim of RAD-AR is for functionality to be expanded in the future by technicians and scientists working in Radiotherapy possessing general computer programming skills, not necessarily by an AR expert, hence low level programming experience should not be a pre-requisite, so we added as meta-requirement (i.e. a specification at the more abstract level of software development) that low level programming should be avoided. Portability to other platforms was another meta-requirement. Considering these meta-requirements we decided to base the development process on Unity, a multiplatform environment for 2D and 3D entertainment games and serious games ("Serious Games Definition from Financial Times Lexicon," 2016) development. Xcode was used to deploy RAD-AR to iOS devices. When the HoloLens became available, direct support was made available in Unity, and MS Visual Studio was used to deploy RAD-AR to the HoloLens.

Several tools were used for intermediate data processing and modelling. The data standard for medical image data is the Digital Imaging and Communications in Medicine (DICOM) standard. One of the most powerful DICOM processing applications, covering almost all our project's needs, is OsiriX. Low-level DICOM and imaging data processing was carried out in Matlab. More details are given in Section 3.4.

3.3 Rationale for Hardware Choice

iPad

When we started our research, according to many consumer electronics reviews the Apple iPad was the tablet computer with the highest specifications on the consumer market [95][96]; it was also the most popular tablet computer in medicine ("BMJ Careers - The iPad and medicine," 2016)("Survey: Doctors prefer tablets" 2014). At that time (and probably also at the time of writing) Android devices had lower hardware and optical specifications, hence we decided to adopt the iPad as our main development platform, while keeping portability to other platforms as one of the main requirements. Although some studies pointed out potential uses of smartphones in medicine (Ozdalga, Ozdalga, & Ahuja, 2012)(Boissin, Blom, Wallis, & Laflamme, 2017), smartphones were not considered as the smaller display size, compared to tablets, would have brought no advantages and would have only been a source of inaccuracy and user interaction problems, e.g. in perception of 3D features (Dey, Jarvis, Sandor, & Reitmayr, 2012). A preference for tablets over smartphones for clinical tasks has also been reported in the literature ("Survey of physicians suggests tablets more useful than smartphones," 2016).

HoloLens

Microsoft HoloLens is an optical see-through head mounted display and the first device using the windows holographic platform; it is only available under the Windows 10 operating system and was released to developers in 2016. The HoloLens is a platform developed by Microsoft specifically for mixed reality. It is able to execute applications integrating virtual elements (Microsoft refers to "holograms"; strictly speaking it is video AR content ("Microsoft HoloLens: Not holograms," 2018)) within the real space. It is also the first fully untethered AR headset, featuring the highest angular resolution and the largest eye-box in the industry. The HoloLens has the first inside-out global sensor fusion system allowing precise head tracking and 3D mapping of the environment, fully controlled by a custom designed on-board GPU (Figure 17 and Figure 18).

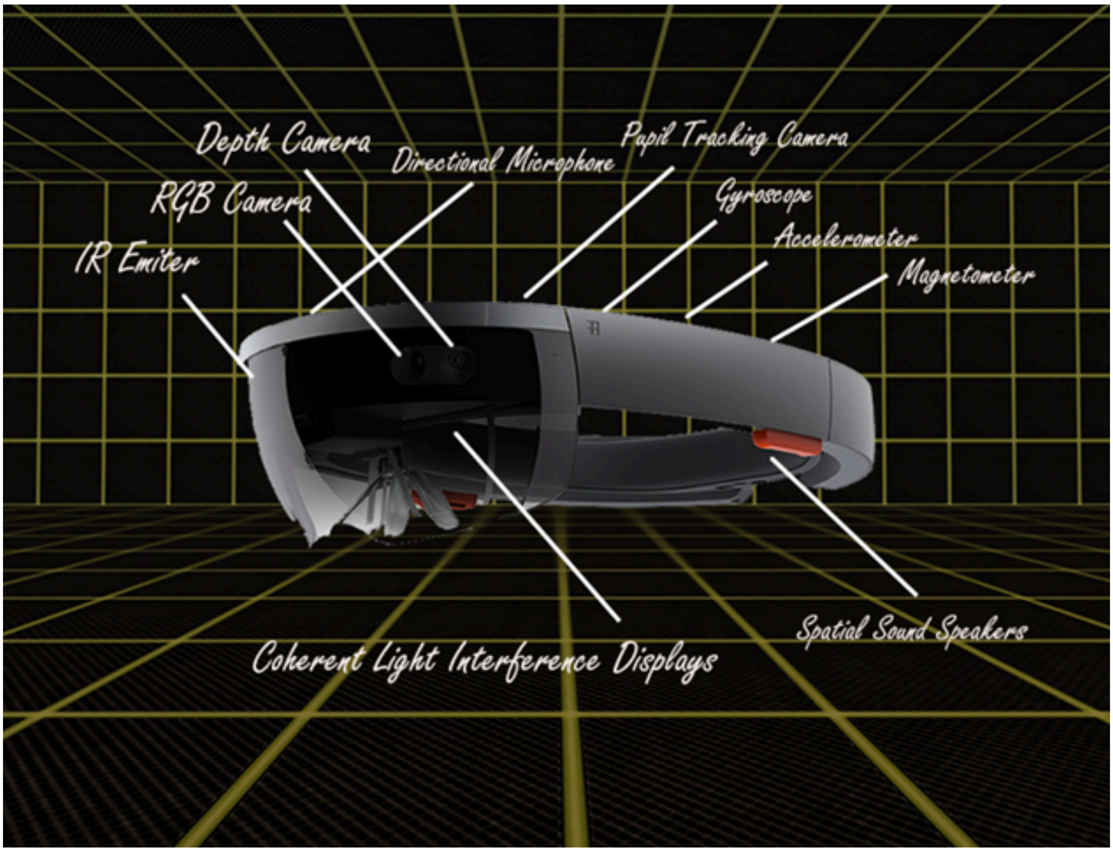


Figure 17 HoloLens sensors location (from ("Top 21 HoloLens Ideas," 2017)**).**

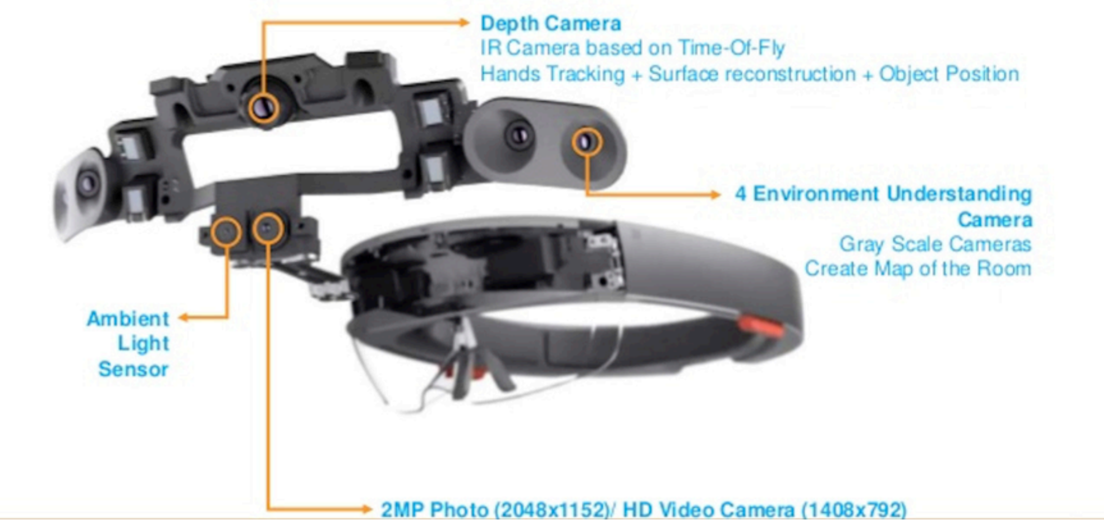


Figure 18 HoloLens sensor assembly (from ("HoloLens hardware details," 2017)**).**

For a description of the technology we refer to (Kress & Cummings, 2017) and ("Top 21 HoloLens Ideas," 2017). Medical applications of the HoloLens were considered amongst its main applications since the product launch ("HoloLens, MD," 2017), so we decided to deploy RAD-AR to the HoloLens and include it in our research as soon as the device became available to our research group.

3.4 RAD-AR: Implementation Details

Software engineering aspects

In order to check correctness, robustness, and efficiency of code RAD-AR was developed adhering to the relevant software engineering best practice principles:

- version control was implemented in Git ("Git");
- the following testing techniques: black box and white box testing (strictly speaking we used techniques inspired to these, as the tester and the developer were the same person, the author), unit testing, incremental integration, and performance/load testing were applied alongside with each development step;
- the development methodology chosen from the beginning privileged portability, expandability of the system, and avoidance if possible of low level programming and data processing.

Development of RAD-AR required use of the following development platforms and software tools: Unity, Vuforia, Visual Studio, Xcode, OsiriX Lite, Matlab, and HoloLens SDK.

Unity

Unity (developed by Unity Technologies, San Francisco) is one of the most widely used game engines. Use of Unity as the main development platform for RAD-AR allowed the portability, modularity, expandability and robustness requirements to be satisfied. Unity includes a cross-platform development environment and can be used to develop video games and simulators for PC, consoles, mobile devices and websites. Unity covers, at the time of writing, 29 platforms (“Unity - Multiplatform,”), putting the emphasis on portability. Supported platforms include Android, Apple TV, BlackBerry, iOS, Linux, Nintendo 3DS, macOS, PlayStation, Unity Web Player, Wii, Xbox, Windows Phone and Windows.

Unity can be considered a *de facto* industry standard for developing interactive 3D content as witnessed by the fact that a number of major computing firms have elected Unity as native development platform for some of their main products, like Microsoft HoloLens, and Oculus Rift, HTC VIVE, Google Cardboard/Daydream, etc. The engine supports most of the main graphic APIs (Direct3D, OpenGL, OpenGL ES, etc.) and implements many advanced 3D computer graphics techniques (e.g. bump mapping, reflection mapping, parallax mapping, screen space ambient occlusion, dynamic shadows, render-to-texture, etc.).

The RAD-AR Unity project was structured as follows. 3D models of anatomical structures were created in OsiriX (described later in this section) and exported in Wavefront OBJ format (“Wavefront .obj file,” 2018). Empty game objects were initially created and named in a representative way to group graphic or functional content that was logically coherent (screenshots in Figure 19 and Figure 20):

- The *Patient* game object includes as sub-objects all the graphical content extracted from the patient’s medical imaging data (CT scans in the current implementation, but, with little effort, it could be replaced or complemented by imaging from any modality - MRI, PET, ultrasound);
- The *Beam* game object groups together the game objects used to display treatment fields: spot light representing open x-ray fields, opaque blocks representing field collimators, opaque strips representing MLC leaves;

- The *Controls* object collects all the control elements: sliders controlling position, orientation, size and transparency of the relevant Field and Patient sub-objects; buttons toggling on/off rendering of graphic objects;
- Other objects are specific to the AR SDK (e.g. ARCamera, etc.).

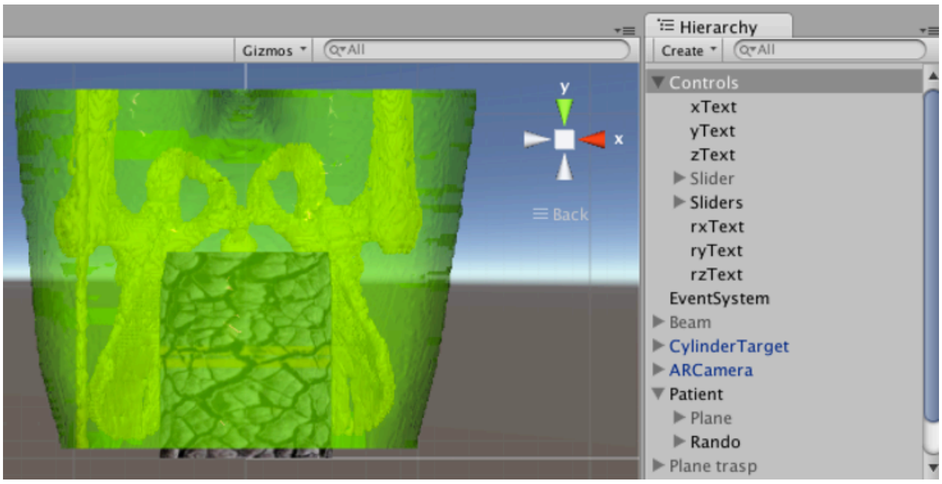


Figure 19 Screenshot of Unity scene windows of RAD-AR iPad version. The following elements are visible: Cylinder marker (covered by Vuforia "tarmac" pattern), anthropomorphic radiotherapy phantom (RANDO) body outline and bone structures.

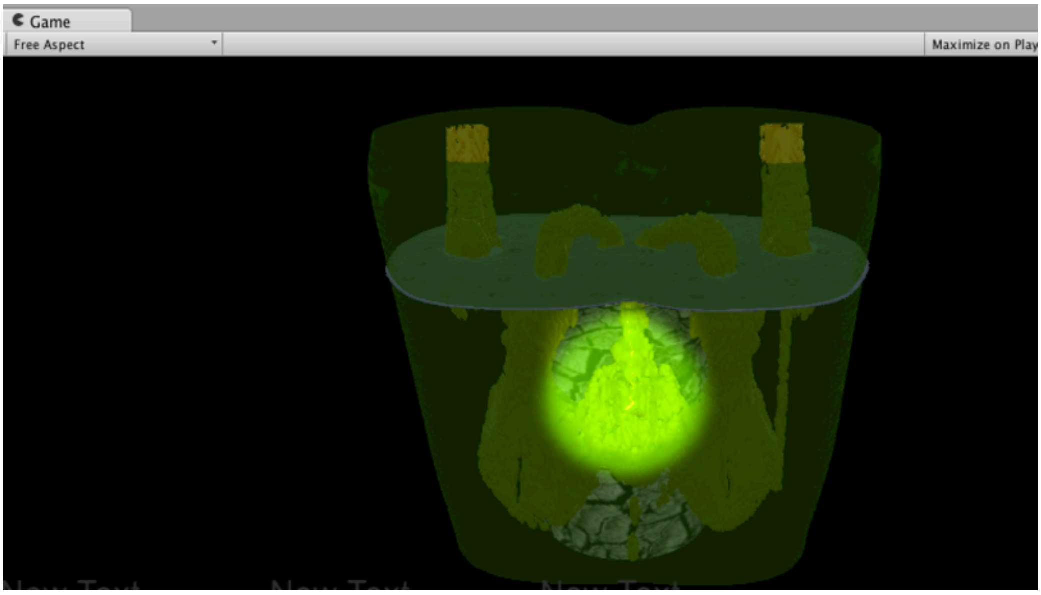


Figure 20 Screenshot of Unity game windows of RAD-AR iPad version. The following elements are visible: Cylinder marker, anthropomorphic radiotherapy phantom (RANDO) body outline and bone structures, and intersection of radiation beam with RANDO structures.

Most graphical features needed custom implementation using shaders for surface rendering and materials, and C# scripts for control elements and some graphic effects. Shaders were attached to materials and C# scripts were attached to the game object with the most intuitive logical relation to the script. For example, the function allowing to *open a hole* of size controllable by the user in the patient skin to see structures inside was implemented as a set of C# scripts (MoveSphereWithCamera.cs, SetRenderQueue.cs, SphereSize.cs, Figure 21 to Figure 24) generating a sphere with fully transparent material used for surface rendering, exploiting the render queue attribute in the implementation of materials. The C# scripts were attached to the AR camera game object. A sphere assigned a transparent material and is rendered after the components that we want to see inside the hole (CT slices, anatomical structures outlines) and before the patient the body. The sphere moves together with the ARCamera, on the focal axis at 0.1 m in front of the focal point. When the camera points at the patient the sphere is rendered in front of the Patient object. The sphere is rendered by a shader ("Masked/Mask", Figure 25) that sets ColorMask to zero, preventing writing to the RGBA channels to objects rendered after the sphere. The sphere is rendered after regular geometry but before masked objects. The overall effect is to generate a hole in objects rendered after the sphere. The angles used are coded by default by quaternions, so a conversion to Euler angles was needed.

```
using UnityEngine;
using System.Collections;
[AddComponentMenu("Effects/SetRenderQueue")]
[RequireComponent(typeof(Renderer))]
public class SetRenderQueue : MonoBehaviour
{
   public int queue = 1;
   public int[] queues;
   protected void Start()
   {
      if (!GetComponent<Renderer>() || !GetComponent<Renderer>().sharedMaterial || queues == null)
         return;
      GetComponent<Renderer>().sharedMaterial.renderQueue = queue;
      for (int i = 0; i < queues.Length && i < GetComponent<Renderer>().sharedMaterials.Length; i++)
         GetComponent<Renderer>().sharedMaterials[i].renderQueue = queues[i];
   }
 }
```

Figure 21 SetRenderQueue **C# script. The script is attached to the sphere object that we use to "open a hole" on object surfaces. A sphere is rendered in a relative position fixed in front of the AR camera. The sphere is rendered using a transparent material that in practice renders the background on the sphere. In Unity the order in which objects are drawn is defined using the Queue tag. A Shader decides which render queue its objects belong to. Usually any transparent shaders make sure they are drawn after all opaque objects and so on. We exploited this possibility by rendering the shader used for the sphere transparent material to render it after all opaque objects on which we don't want to make a hole through (they are considered by the rendering engine as background for the sphere), and before all opaque objects through which we want to make a hole.**

```
 using UnityEngine;
using UnityEngine;
using System.Collections;
using UnityEngine.UI;
public class SphereSize : MonoBehaviour
{
        public float size = 0.0f;
        public Slider sizeSlider;
        public GameObject sphereObject;
        void Start () {}
        void Update ()
    {
                sphereObject.transform.localScale =  new Vector3(0.05f * sizeSlider.value, 0.05f *
sizeSlider.value, 0.05f * sizeSlider.value);
        }
}
```

Figure 22 SphereSize **C# script.** sphereObject.transform.localScale **sets the sphere size (i.e. the hole size) using the value of a slider control** sizeSlider.value**.**

```
using UnityEngine;
using System.Collections;
public class MoveShpereWithCamera : MonoBehaviour {
public GameObject sphere;

void Start (){}
void LateUpdate ()
    {
                transform.position = player.transform.position +
Quaternion.Euler(player.transform.rotation.eulerAngles) * new Vector3(0.0f, 0f, 0.1f);
    }
}
```

Figure 23 MoveShpereWithCamera **C# script.** Quaternion.Euler **returns a rotation that rotates around the z axis, x axis, and y axis. z axis points in front of the camera. The rotation is applied to the vector** Vector3(0.0f, 0f, -0.1f)**, a vector 0.1 m long, pointing in the direction of the z axis. The script is attached to the game object AR camera. The position of the** GameObject sphere **is changed in such a way to keep it in front of the AR camera at a distance of 0.1 m.**

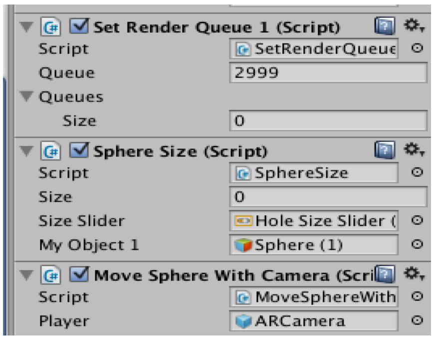


Figure 24 The SetRenderQueue **and the** MoveSphereWithCamera **C# scripts are attached to the transparent sphere object determining its position (always 0.1 m in front of AR the camera) and render queue.**

```
Shader "Masked/Mask" {
    SubShader {
// Render the mask before masked geometry and
// transparent things and after regular geometry.
        Tags {"Queue" = "Geometry+10" }
        // Don't draw in the RGBA channels; just the depth buffer
        ColorMask 0
        ZWrite On
        // Do nothing specific in the pass:
        Pass {}
    }
}
```

Figure 25 ShaderMask **shader. Renders the mask after regular geometry, but before masked geometry an transparent things. Does not draw in the RGBA channels, just the depth buffer.**

AR SDKs for iOS

After a preliminary investigation of several AR SDKs (section 3.2) we decided to start the development of RAD-AR based on Vuforia and Metaio. Both AR SDKs selected to develop the iOS version of RAD-AR are fully supported in Unity. Unity is one of the recommended development platforms by both the manufacturers of Metaio and Vuforia. Apple acquired Metaio in 2015 and support and updates to the SDK are now discontinued. Due to discontinuation of support and updates for Metaio we decided to implement the most recent developments of RAD-AR for Vuforia only.

In 2017 Apple released ARKit, an AR SDK for iOS 11, which partly builds on Metaio. Google has released ARCore, an AR SDK for Android. Plans to investigate use of these SDKs will be discussed in 7.3.

Visual Studio and Xcode

Visual Studio and Xcode are the main programming development environments for HoloLens and iOS and have been used to build the executable code for RAD-AR. Preconfigured projects for Visual Studio and Xcode are generated by Unity and only need a build phase carried out by Visual Studio and Xcode.

OsiriX Lite

3D models in OBJ format used in RAD-AR were generated in OsiriX Lite, the free version of OsiriX, one of the most widely used DICOM viewers by medical practitioners. Also patient anonymization was carried out in OsiriX Lite. To generate OBJ models for an outlined structure (e.g. rectum, prostate, PTV) a CT dataset was generated from the original one, setting to 100 (-100) the CT values of voxels outside (inside) the structure and extracting the 3D surface with voxel threshold 0. The 3D surface was then exported as Wavefront OBJ model.

Matlab

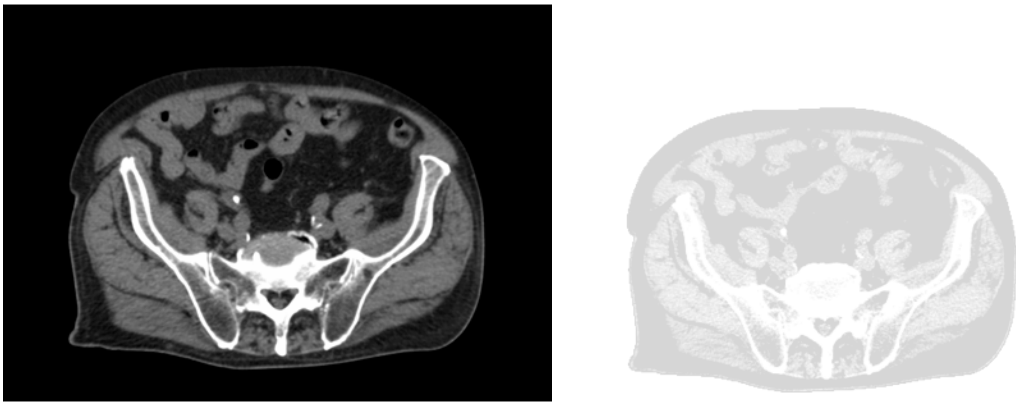
Being one of the most powerful mathematical development environments, with particularly efficient matrix data support, Matlab was the platform used when low level imaging data processing was needed. We used Matlab to deal with image transparency (alpha channel manipulation), image interpolation or resolution coarsening, histogram and contrast management (Figure 26 and Figure 27).

```
% pre-process CT images -> one block of n_thick_slice images from top image
% for each original CT slice
% e.g. for 74 original slices and thickness of 8 slices
% slice_1 -> slice_im_1_1, ...,slice_im_1_8
% ..................................
% slice_74 -> slice_im_74_1, ...,slice_im_74_8
% transparency decreases from  slice_im_74_1 to slice_im_74_8
% and similarly for all blocks from top slice (1) to bottom slice (8)

% initialization
n_CT_slices = 74;

n_thick_slice = 8;
CT_folder = 'F:\G726329\CT.G726329.';
output_folder = 'C:\Users\Francesco\Desktop\G726329\alpha_images\';

% image processing cycle
for j = 1:n_CT_slices - n_thick_slice
   for i = 1:n_thick_slice
```

```
        % read CT slice
        slice_image = dicomread(strcat(CT_folder,int2str(i+j-1),'.dcm'));
        % crop CT slice
        slice_image = slice_image([1:400],:);
        % binary mask for body
        mask = double(imfill(im2bw(slice_image,0.01),'holes'));

        % alpha decreasing from top to bottom slice in slices block
        alpha = double(0.0+(double(i-5)/43))

        % image histogram rescaled to spread gray values on visible range
        slice_contrast_adjusted = imadjust(slice_image, [0.0153; 0.017], [0; 1]);

        % writes semitransparent CT slices blocks
        % with alpha decreasinf from top to bottom
          imwrite(slice_contrast_adjusted,strcat(output_folder,...
                'slice_im_', int2str(j+11),'_',int2str(i+j-1),'.png'),...
                'png','Alpha',alpha*mask);
    end
end
```

Figure 26 Matlab code processing CT slices for pseudo volume rendering. 81 slices are processed and 74 sets of 8 slices (slice n. 1-8, 2-9, …, 74-71) are produced with transparency decreasing from first to last slice in each set.

Figure 27 Each line shows a set of 8 slices processed with the Matlab script in Figure 26. Transparency decreased from leftmost (1st slice in each set) to rightmost (8th slice in each set). On each row the value of the vertical coordinate decreases by 0.3 cm. Each set of 8 slices covers a thickness of 8 x 0.3 cm (2.4 cm) producing a volume rendering effect if observed from the top. The fist CT slice on one row is the second on the line above, the third on the second line above, and so on.



(a) (b)

Figure 28 (a) Unprocessed CT slice. (b) CT slice with background removed and made semitransparent after processing with the Matlab script in Figure 26.

HoloLens

The development environment for the Microsoft HoloLens is entirely Windows based and native support is available in Unity. A Visual Studio preconfigured project is built by Unity and needs to be built in Visual Studio to generate the HoloLens app.

The rendering capabilities supported by the HoloLens SDK are essentially those inherited from Unity, so only surface rendering is immediately available for the HoloLens. Visualization in 3D of the CT dataset could benefit from volume rendering (Calhoun, Kuszyk, Heath, Carley, & Fishman, 1999). Volume rendering of the CT dataset is available in some commercial software used in radiotherapy for desktop workstations, e.g. the Varian Eclipse treatment planning system. Volume rendering for the HoloLens is a research topic in itself and outside of the scope of this thesis as it would involve intense use of low level code development (something that we wanted to exclude to privilege portability, see section 3.2); we decided to investigate volume visualization using a simplified approach. CT slices are rendered as semi-transparent objects in the Unity scene, registered to the 2D outlines of the patient's anatomical structures (Figure 29). The following types of semi-transparent rendering were implemented using the alpha channel of the CT slice exported in PNG (Portable Network Graphics) format:

- the alpha channel source comes from the grey scale of the image;
- the alpha channel is constant for all CT slices;
- the alpha channel is constant for each single slice but varies from one slice to another with transparency reducing from the top to the bottom slice (it is assumed that the user observes the dataset from the top with respect to the vertical axis).

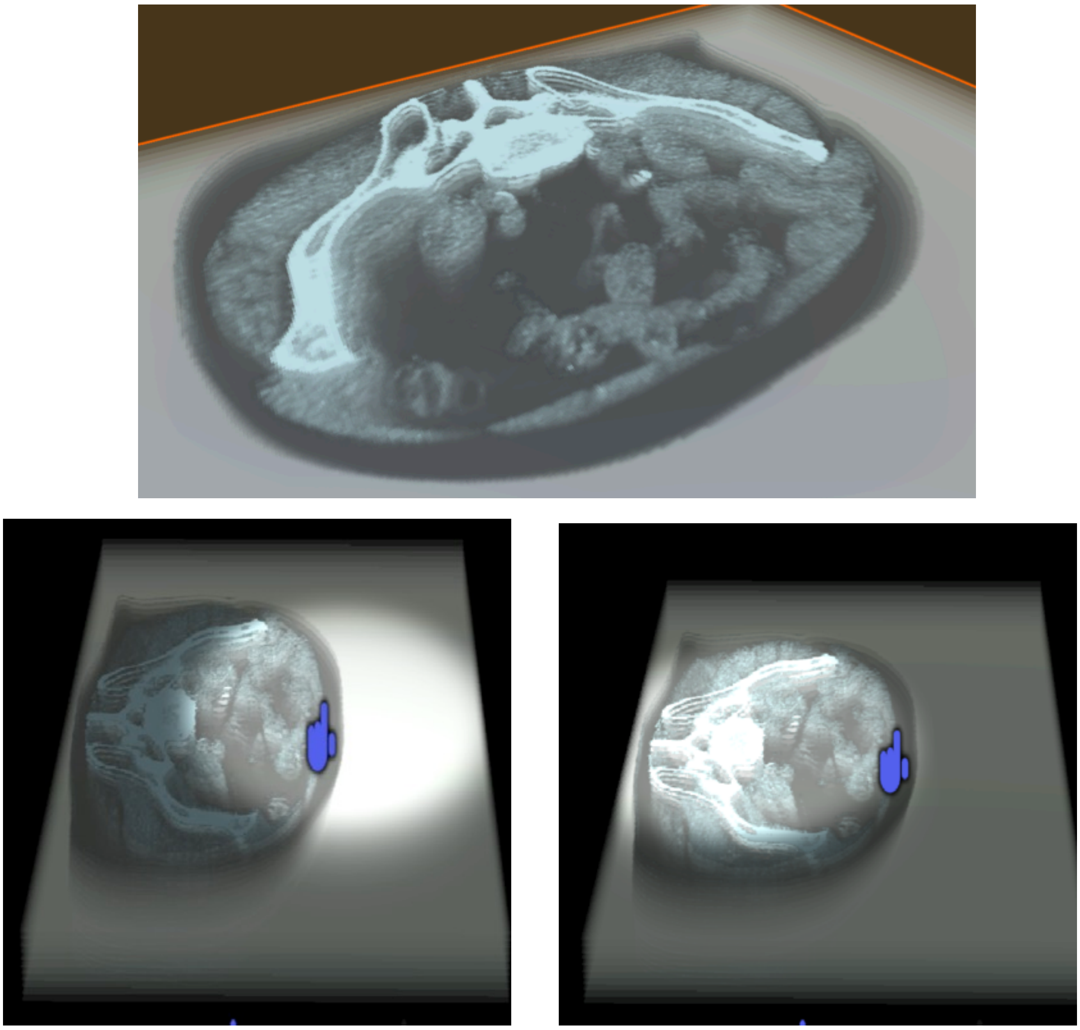


Figure 29 Pseudo volume rendering; 8 semitransparent CT slices are rendered with transparency decreasing form the top to the bottom (top). Use of spotlight Unity game object to control contrast/luminosity of CT dataset rendering without low-level data processing (bottom). The blue object is the HoloLens gaze cursor.

A major aspect of the HoloLens version of RAD-AR is the implementation of visualization controls (magnification, position and rotation of virtual content, switching on/off visualization of structures, CT dataset navigation). Controls can be implemented as gestures and vocal controls, or as Unity 2D interface controls. We used a mix of the gestures and Unity 2D interface controls: position control is implemented as hand gestures, other controls (magnification, rotation, visual effects, etc.) as 2D controls (sliders, selection lists, etc.). The choice was dictated by robustness end ease of use requirements; e.g. rotation could be implemented as user's head rotation gesture, but this was noted to produce unwanted rotation of the AR content as involuntary head rotations occur when the user concentrates on hand gestures to change the AR content position. Controls built from scratch from unity game object were also implemented to allow customization of the interface and portability to other HMD platforms. We investigated also the implementation of rotation as gesture (linked to the user head position). Vocal controls were not considered, as they would add unnecessary complexity, being only interested in understanding, at this stage, graphics aspects of AR in relation to radiotherapy.

Structure Sensor

The Structure Sensor (Occipital, Inc., San Francisco, CA, USA, ("Structure Sensor," 2018)("Teardown Tuesday," 2018)) is an optical system designed for the iPad capable to acquire a 3D model of physical objects in the real scene, of the whole real scene, or of part of it. We used the Structure Sensor to acquire 3D models of the RANDO in its original shape and with body changes simulating changes in patient weight, implemented with conformal treatment bolus sheets of 0.5 cm and 1.0 cm thickness. 3D models in OBJ format are exported directly from the model scanner iPad application provided by the sensor's manufacturer.

Figure 30 The Structure sensor (Occipital, Inc., San Francisco, CA, USA).

3.5 RAD-AR: Summary of Features and Experiments

The outcome of the software development stage was RAD-AR, a software framework for radiotherapy AR applications. Based on RAD-AR we developed three software applications able to display, as augmented reality content, organs and treatment area outlines, CT slices (and volume data), and features of radiotherapy plans, e.g. treatment beams, isodose surfaces, and shielding devices. The applications share the same design philosophy, basic functionalities, and software components. Each application builds on RAD-AR, adding functionalities targeting the following radiotherapy specific uses (listed in chronological order of implementation and experimental testing):

- patient treatment setup
- patient education
- treatment plan visualization/evaluation.

The functionalities specified in section 3.1 were all implemented and tested. In Chapter 4, Chapter 5, and Chapter 6 we will consider experimental testing of the three tools developed. Quantitative experiments were performed to evaluate performance of the treatment setup tool, and a user feedback study was carried out to evaluate usability of the patient education and the plan visualization tool.

Chapter 4. Clinical Tool for Patient Treatment Setup

4.1 Experimental Evaluation

Two important aspects of virtual content visualization with RAD-AR are first considered:

- registration of virtual content with the real-world scene in terms of accuracy and precision of camera pose (section 4.2)
- fidelity of virtual content geometric representation in the real scene (section 4.3).

We will refer to accuracy and precision following the use accepted in physics (JCGM, 2008) (Figure 31).

- Accuracy quantifies systematic error in a measurement, i.e. how close the result, usually calculated as the mean value of a set of repeated measurements of a quantity, is to the true value of the quantity, measured by a reference procedure and reference instruments accepted by definition as free from systematic error (the meaning in computing is similar; accuracy is the nearness of a calculation to the true value).
- Precision quantifies the degree of agreement amongst a series of repeated measurements of a quantity; precision can also be interpreted as a measure of repeatability and reproducibility of results with no reference to accuracy. The measure of precision is commonly computed as the standard deviation of the dataset. Less precision is reflected by a larger standard deviation (in computing, precision is the resolution of the representation, typically defined by the number of decimal or binary digits).

The ISO standard defines the same concepts with a different terminology; the above defined terms “accuracy” and “precision” are referred in the ISO standard as “trueness” and “precision” respectively, using the term “accuracy” for the pair trueness/precision of concepts as a quantification of the quality of a measurement (“ISO 5725-1:1994(en), Accuracy”).

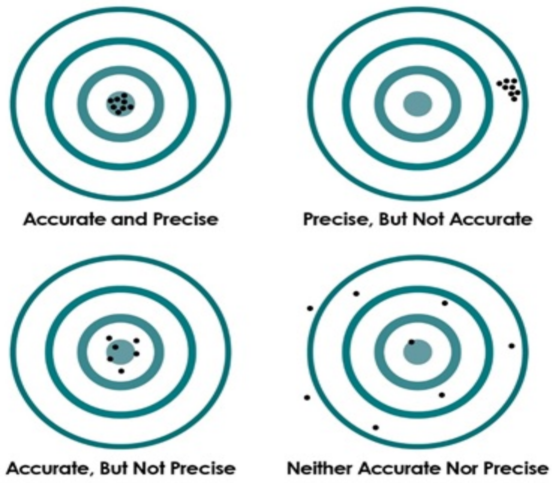


Figure 31 Visual explanation of meaning of Accuracy and Precision in physics.

Experiments were performed to estimate accuracy and precision of camera pose and precision (repeatability and reproducibility) of a patient set-up procedure based on our software (section 4.4).

4.2 Camera Pose Accuracy and Precision

4.2.1 Materials and Methods

In this section we describe the work carried out on measurement of camera pose accuracy and precision for Vuforia and for the HoloLens SDK. Camera pose is the process of calculating the relative position and orientation of the viewing component (back camera for tablets, user eyes for HoloLens) in an environment. Camera pose is essentially a measurement process; it is based on photogrammetry for the marker based SDK used for iPad development and environment mapping and physical sensors readings (gyroscope, accelerometer, etc.) for the HoloLens. In a recent study (Belhaoua, Kornmann, & Radoux, 2014) the more general problem of feature detection and tracking and the impact on camera pose precision is considered. The authors performed a measurement of the accuracy of the edge detection process for a marker based AR system. The edge detection error is mathematically propagated to the main aspects of the registration process up to the final tracking step. Our approach was different as we were not interested in understanding the source of errors; we were only interested in an estimate of accuracy and precision to inform the choice of the software framework; we considered only the results of the final tracking step. For a set of known physical positions of the device, we have read the camera pose parameters calculated by the device and compared them to physical measurements of the same quantities. The experimental setup is illustrated in Figure 34 to Figure 37.

Vuforia offers several choices for the geometry of tracking markers: flat image, cube, parallelepiped, cylinder, 3D object (Figure 32). We decided to use a cylinder marker as it performed better than other options in a preliminary comparison carried out with a cylinder and a cube marker (the cube marker introduces an error of about 1 mm when the self tracking algorithm – tracking on face at the time – switches form one face of the cube to another one). Better results were also obtained in regards to size and shape of the region of space where the iPad could be used without losing track of the marker, and showed highest stability of self-tracking (3D work better than 2D markers, and markers with more edges are less stable – show flickering effects – when the self-tracking algorithm switches tracked face, hence the cylinder, having only 2 edges - or 1 when sitting on a surface - provided greater stability). We used a pattern provided by the manufacturer ("tarmac" pattern Figure 33).

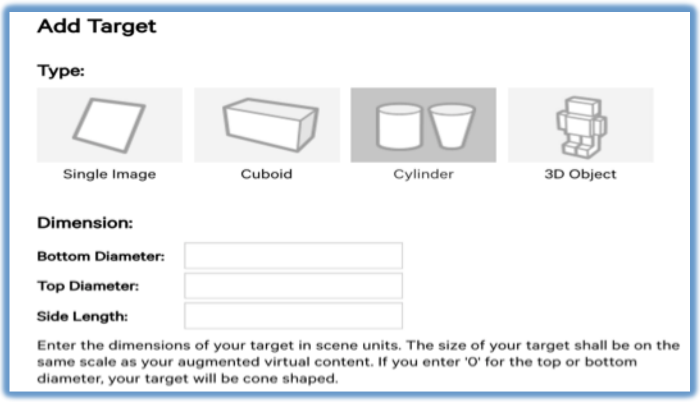


Figure 32 Markers for self-tracking supported by Vuforia ("Target Manager | Vuforia," 2018)**.**

Figure 33 Vuforia "tarmac" pattern; side of cylinder target ("Target Manager | Vuforia," 2018)**.**

The device (iPad or HoloLens) was mounted on a mechanical stand (Figure 34). The world reference frame used for camera pose estimate by the self-tracking algorithm for the iPad is located at the centre of the marker (Figure 34 and Figure 36); the initial configuration is setup such that the camera pose estimates x = 0 (rotating the orientation of the cylinder around the z axis) and z = 0 (adjusting the vertical position of the iPad's stand). The origin of the world reference frame ("Coordinate systems," 2018) for the HoloLens is the location of the camera focal point when the application starts; x, y, and z directions are horizontal left/right, horizontal front/back, and vertical down/up. The device is constrained to move on straight lines by means of a rail mechanism. Rotation of the device around the vertical axis was also possible with a resolution of 0.5°. Shifts of the support along the constraint direction could be measured with a resolution of 1 mm.

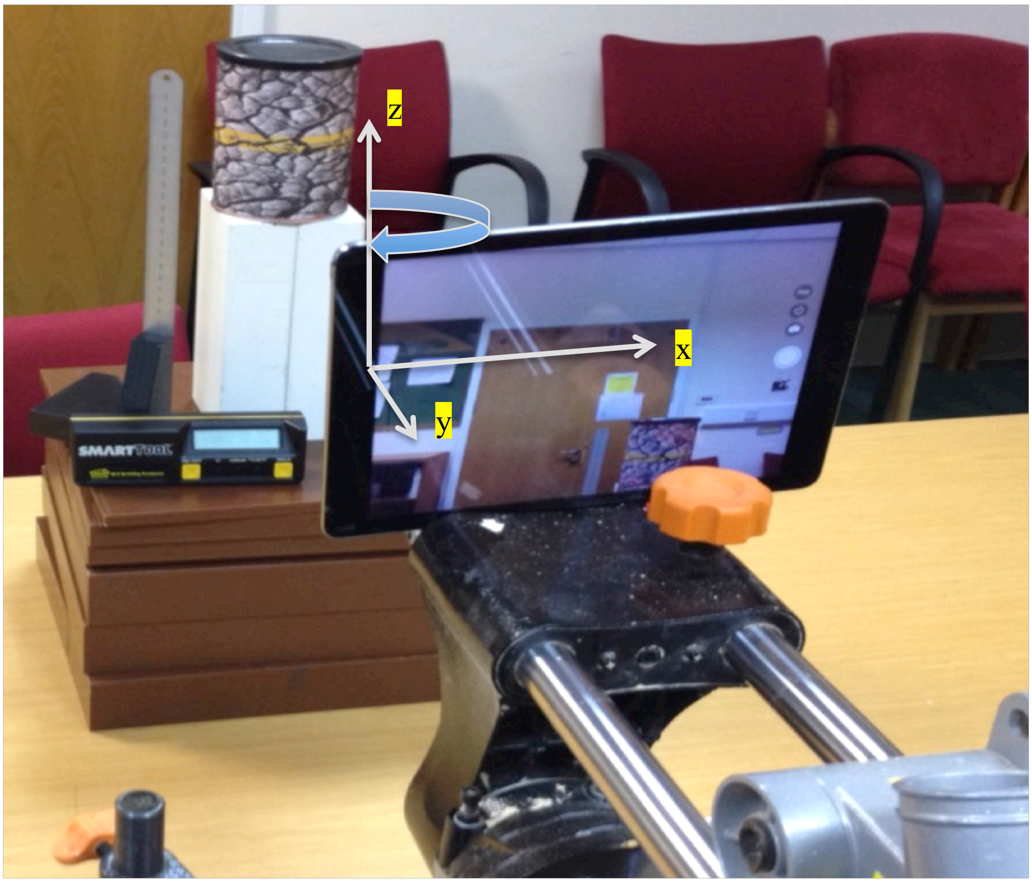


Figure 34 Measurement of self-tracking accuracy and precision for iPad version of RAD-AR with the iPad anchored to a mechanical stand allowing controlled and measurable shift in the horizontal direction, and rotation around the vertical axis. Vertical and longitudinal shifts were implemented translating the whole stand. Allowed shifts and rotation shown by arrows in the picture.

In order to evaluate camera pose accuracy the device was moved in intervals of 5 mm along the x direction and the camera pose Cartesian coordinates and angles as estimated by the device were read by the software. The process was repeated after application of displacements of 5 mm in y and z direction. The result was a 3D array (indexed by the three Cartesian coordinates with 5 mm steps in each direction) of pairs $(P, R)_{X,Y,Z}$ where:

- X, Y, and Z are the coordinates of the device's camera as measured mechanically from the tracks/stand/ruler system
- $P = (p_x, p_y, p_z)$, where p_x, p_y, and p_z are the camera pose Cartesian coordinates
- $R = (r_x, r_y, r_z)$, where r_x, r_y, and r_z are the camera pose angles

with P and R estimated by self-tracking.

Sets of measurements were acquired changing the device orientation and angle around the vertical axis in 1° increments for angles ranging from -30° to 30°.

Differences between mechanical measurements (considered the true values) and software estimates of camera pose parameters are used to estimate the accuracy of self-tracking component of the system. The errors originate from approximations made in the self-tracking algorithms of the physical parameters characterizing the optical components, and from mathematical approximations in the algorithms.

In order to evaluate precision the device support was set to a fixed position with the device mounted on to the support; the support was moved and put back in the same position (15 times), and readings of the camera pose parameters estimated by the device was acquired by taking an automated reading 5 sec after the support was put back to allow vibrations due to mechanical motion to fade, and mechanical stress to settle. The support was moved to 37 different fixed positions with shifts of 2.0 cm and 2° and the procedure repeated.

A second set of measurements reproducing the experiment performed with the stand was acquired with the device fixed on the LINAC treatment couch (the treatment couch has a position and horizontal angle motorized control mechanism, with resolution of 0.1 mm and 0.01°, Figure 35 to Figure 37).

Figure 35 Measurement of self-tracking accuracy and precision for iPad version of RAD-AR. The iPad is anchored to the LINAC treatment couch.

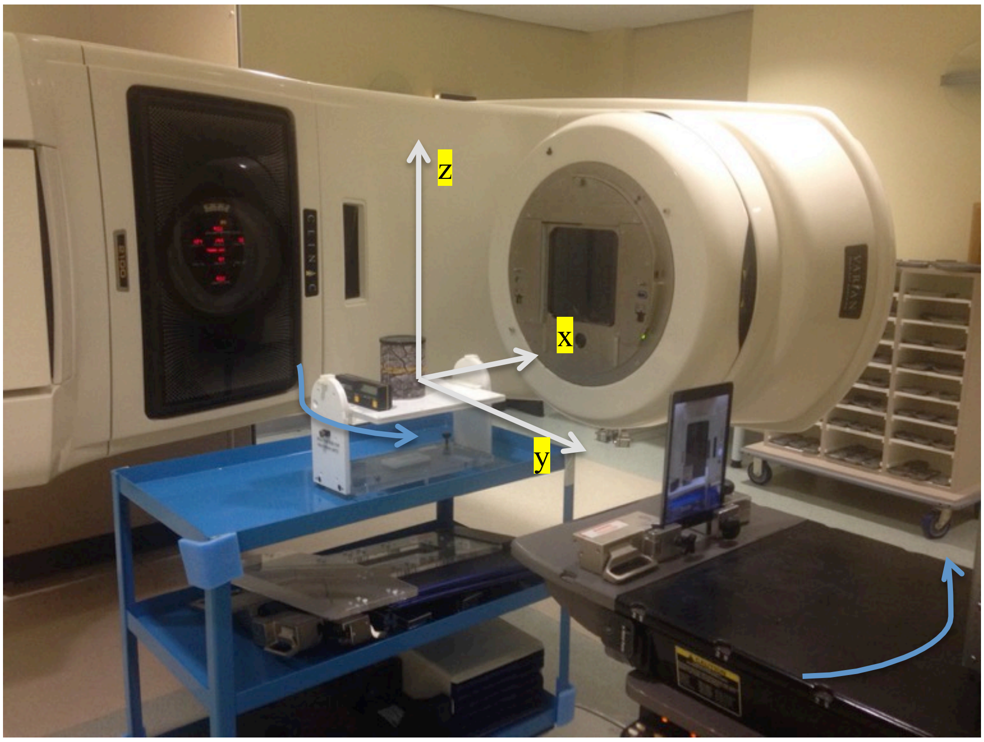


Figure 36 Measurement of self-tracking accuracy and precision for iPad version of RAD-AR. The iPad is anchored to the LINAC treatment couch. The couch can be shifted along the three orthogonal directions and rotated around the vertical axis as indicated by the arrows in the picture.

Figure 37 Measurement of self-tracking accuracy and precision for iPad version of RAD-AR. The iPad is anchored to the LINAC treatment couch. Complete view.

4.2.2 Results

Accuracy is quantified by camera pose errors, i.e. the differences between mechanical measurements and software estimates for each camera pose parameter; accuracy changes depending on the device's position (Figure 38 and Figure 39).

iPad

Figure 38 and Figure 39 show a sample of results for the iPad self-tracking error E for:

- x = -25.0 to 25.0 cm, y = 25.0 cm, z = 0.0 cm (Figure 38)
- x = - 25.0 to 25.0 cm, y = 35.0 cm, z = 15.0 cm (Figure 39).

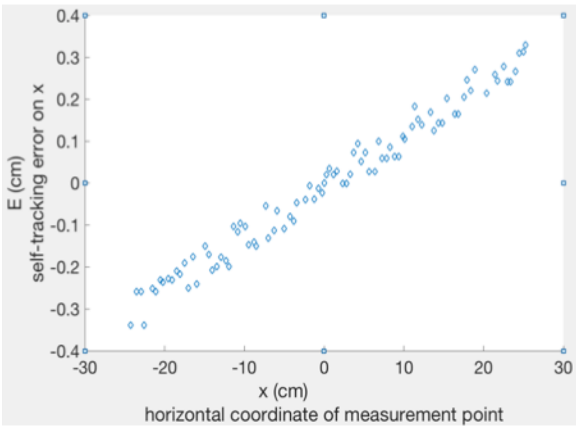


Figure 38 Self-tracking error (quantifying accuracy) of x coordinate estimate for the iPad (x = -25.0 to 25.0 cm, y = 25.0 cm, z = 0.0 cm). The amplitude of the noise in the graph is related to precision (reproducibility).

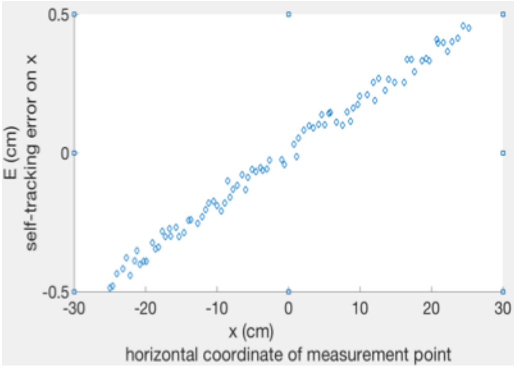


Figure 39 Self-tracking error (quantifying accuracy) of x coordinate estimate for the iPad (x = -25.0 to 25.0 cm, y = 35.0 cm, z = 15.0 cm). The amplitude of the noise in the graph is related to precision (reproducibility).

The self-tracking error increases (accuracy deceases) as the marker distance from the camera increases and when the marker image approaches the edge of the 2D camera view. A linear trend of the error can be observed, suggesting a systematic error (affecting accuracy), with noise superimposed with amplitude of approximately 1 mm. The amplitude of the noise is related to precision; the noise is random error superimposed to camera pose estimates at different positions, precision is random error superimposed to camera pose estimates at the same position. Measurements were repeated replacing the iPad used to acquire the first dataset with another iPad of the same model; a linear trend with slightly different slope was observed. The difference can be explained considering that the devices are not individually calibrated at the factory and identical manufacturing specifications are assumed; this view is supported by the fact that Apple is now calibrating iPhone 8 cameras individually at the factory to improve AR capabilities (“iPhone Cameras,” 2018). This type of systematic error can be corrected by software after calibration of the device optics but a consideration of this type of issues is beyond the scope of this thesis.

Mean values of camera pose errors (accuracy), calculated mediating on the whole dataset (x = -25.0 cm to 25.0 cm, y = 20.0 cm to 40.0 cm, z = -25.0 to 25.0 cm) in x, y, and z direction were 0.32 cm, 0.25 cm, and 0.30 cm respectively for the dataset acquired with the mechanical stand, and 0.31 cm, 0.34 cm, and 0.28 cm for the dataset acquired with the motorized couch.

Camera pose precision for x, y, and z direction was 0.07 cm, 0.08 cm, and 0.08 cm respectively for the dataset acquired with the mechanical stand, and 0.11 cm, 0.10 cm, and 0.09 cm for the dataset acquired with the motorized couch.

For the dataset acquired with the mechanical stand, camera pose angle accuracy was 0.7° and camera pose angle precision was 0.4°.

For the dataset acquired with the motorized couch, angle accuracy was 0.8° and angle precision was 0.8°.

HoloLens

Mean values of camera pose errors (accuracy) for the HoloLens, calculated from the whole dataset (x = -25.0 cm to 25.0 cm, y = -10.0 cm to 10.0 cm, z = -25.0 to 25.0 cm) in x, y, and z direction were 0.8 cm, 0.7 cm, and 0.8 cm respectively, for the dataset acquired with the mechanical stand, and 0.9 cm, 0.9 cm, and 0.7 cm respectively, for the dataset acquired with the motorized couch.

Camera pose precision for x, y and z direction was 0.12 cm, 0.12 cm, and 0.13 cm respectively, for the dataset acquired with the mechanical stand, and 0.13 cm, 0.13 cm, and 0.12 cm for the dataset acquired with the motorized couch.

For the dataset acquired with the mechanical stand, camera pose angle accuracy was 0.5° and camera pose angle precision was 0.3°.

For the dataset acquired with the motorized couch, angle accuracy was 0.5° and angle precision was 0.5°.

4.2.3 Discussion of Results

For a hand-on survey on camera pose estimation we refer to (Marchand, Uchiyama, & Spindler, 2016).

iPad

Accuracy for the iPad version, about 2-3 mm, was close to the positional error accepted in most radiotherapy techniques. For example in IGRT tolerances of 1 mm to 5 mm are usually allowed (Schmidhalter et al., 2014). Precision of camera pose (about 1 mm) is adequate to radiotherapy applications and is possibly explained by noise coming from the video stream. Results obtained with both the mechanical stand and the motorized couch are similar, reinforcing the assumption that mechanical measurements are free from systematic error.

Results were consistent with published data on accuracy reported in (Palmer et al., 2015), where an AR system developed for ultrasound applications is considered. Camera pose error reported in this work were in the range of 3-4 mm and 0.3°-1.8°. Errors are larger than our estimates; a possible explanation can be the fact that in that work an iPhone (with a smaller display and optical specifications lower than the iPad) was used; this supports the rationale behind our decision to discard implementation on smartphones.

HoloLens

Also for the HoloLens, results obtained with the mechanical stand and the motorized couch were similar also for the HoloLens. Accuracy was between 0.7 mm and 0.9 mm; this is worse than the iPad, but still close to the order of magnitude of accepted tolerances in radiotherapy. Improvements of self-tracking and camera pose are expected as the technology evolves, letting foresee applicability in the clinical setting in a near future.

We haven't found results about the HoloLens camera pose accuracy published in the scientific literature. Web sources ("The Accuracy of HoloLens' slam," (2018)) indicate values of camera pose errors of the order of 1% of the average distance from the room features detected by the device's sensors and used for self-tracking. This is consistent with our results, obtained with the device at a distance of about 0.5 m to 1.5 m from room features (walls, floor, furniture).

Precision of camera pose is of the order of 1 mm, very similar to that of the iPad version and similarly explainable by noise coming from tracking sensors.

Summarizing, errors in camera pose are of the order of magnitude of errors accepted in some radiotherapy procedures, i.e. 1 mm to 10 mm. Precision for the iPad and the HoloLens was similar, of the order of 0.1 cm. Considering accuracy of camera pose, the iPad version of RAD-AR, which is marker based (Vuforia), performed better (error in the region of 0.2 cm to 0.3 cm) than the HoloLens version (error in the region of 0.7 cm to 0.9 cm) that is based on markerless tracking. The two intervals do not overlap so we consider the difference to be significant.

Better performance of camera pose for marker tracking compared to markerless tracking is a known fact in the AR scientific community ("Markerless inside-out tracking," 2017) and results are reported in the scientific literature (Yang, Cho, Soh, Jung, & Lee, 2008), but an analysis of this aspect is out of scope for this thesis.

4.3 Virtual Content Representation

4.3.1 Materials and Methods

Closely related to camera pose error is another important aspect any AR system, the fidelity of the geometric representation of AR content. This was investigated using the following experimental setup for both the iPad and the HoloLens versions of RAD-AR. Three shapes were considered:

- Cube with 12 cm edges
- Parallelepiped 10 cm x 15 cm x 5 cm
- Cylinder of 10 cm diameter and 12 cm height.

Physical objects and virtual models of these shapes were inserted in the app's scene. To estimate the position in the real scene of AR models the device (iPad or HoloLens) was moved by the experimenter around the scene and the physical object was registered with the corresponding AR model, relying on the experimenter's perception about the position of the AR models edges and flat surfaces, considered the features most neatly identifiable and localizable by visual inspection from a suitable user's viewpoint. To measure the separation between vertical opposite faces of the parallelepiped and cube models two vertical rulers anchored to a stand were aligned to opposite faces of the virtual model and the separation between them was measured with a third ruler (Figure 40).

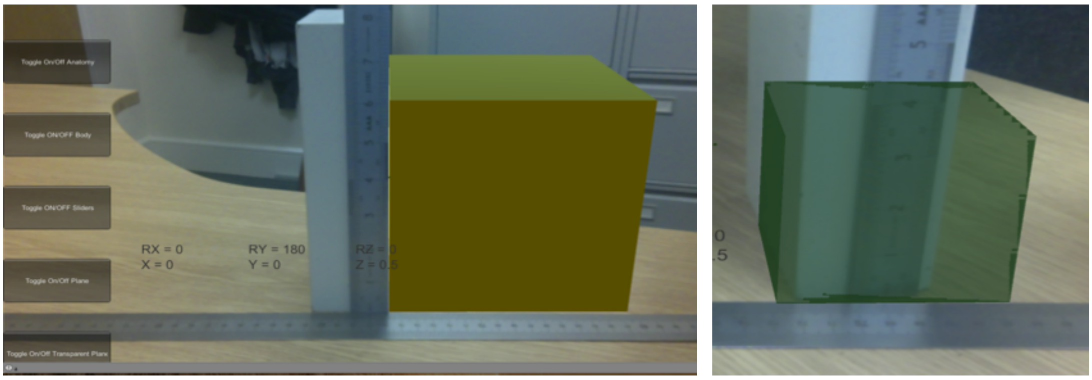


Figure 40 Estimate of AR cube dimensions.

Vertical rulers alignment to edges of the cylinder virtual model was used to estimate the diameter. The height of virtual models was estimated by averaging direct estimates performed with a ruler on opposite faces (for the parallelepiped and the cube) or opposite points on the top face (for the cylinder). The procedure was repeated 20 times for each model, rebooting the AR application. A similar experiment is performed by (Jain, Youngblood, Hasel, & Srivastava, 2017) as part of the evaluation of an anatomy teaching AR tool.

4.3.2 Results

Results of the geometry estimate for the three models used to investigate virtual content placement in the real scene:

Model (1): Cube with 12 cm edges

Model (2): Parallelepiped 10 cm x 15 cm x 5 cm

Model (3): Cylinder of 10 cm diameter and 12 cm height.

for the iPad and the HoloLens versions of RAD-AR are as follows.

iPad

The models rendered by the iPad versions were estimated to have the following geometry (mean over 20 repeated measurements ± standard deviation):

Model (1): Parallelepiped 11.8 ± 0.2 cm x 12.1 ± 0.1 cm x 11.8 ± 0.2 cm

Model (2): Parallelepiped 10.2 ± 0.1 cm x 15.3 ± 0.2 cm x 5.0 ± 0.2 cm

Model (3): Cylinder with 9.9 ± 0.3 cm diameter and 12.3 ± 0.1 cm height.

Reproducibility (precision) of virtual content placement gave the following results: the cube and the parallelepiped model placement on the real scene was precise within 0.15 cm in all directions. The placement of the cylinder model was precise within 0.15 cm in the direction of the cylinder axis and within 0.1 cm in the plane perpendicular to the cylinder axis.

HoloLens

With the HoloLens version of RAD-AR we obtained the following results for the model measured geometry (mean over 20 repeated measurements ± standard deviation):

Model (1): Parallelepiped 11.8 ± 0.3 cm x 11.6 ± 0.4 cm x 11.7 ± 0.3 cm

Model (2): Parallelepiped 9.8 ± 0.3 cm x 14.8 ± 0.4 cm x 4.9 ± 0.3 cm

Model (3): Cylinder with 9.9 ± 0.3 cm diameter and 11.8 ± 0.3 cm height.

Reproducibility of virtual content placement gave the following results: cube and the parallelepiped model placement on the real scene was precise within 0.35 cm in all directions. The placement of the cylinder model was precise within 0.2 cm in the direction of the cylinder axis and within 0.3 cm in the perpendicular plane.

4.3.3 Discussion of Results

Precision of placement of virtual content in the real scene is of the order of 1 mm to 2 mm for the iPad and 2 mm to 4 mm for the HoloLens. Faithfulness of visual geometric representation (i.e. how close the virtual object shape, as perceived by the user, is to the modelled physical object) of virtual content is of the order of 1 mm to 3 mm for the iPad and 2 mm to 5 mm for the HoloLens. Precision of localization is consistent for both systems with the closely related camera pose aspect, for both hardware platforms. In a recent study (Vassallo, Rankin, Chen, & Peters, 2017) a similar problem for the HoloLens is considered in the context of clinical intervention guidance. The authors obtained results similar to ours (localization of content is precise within 3 mm to 5 mm) and conclude that the Microsoft HoloLens shows promise of effectiveness in guiding clinical interventions, but its accuracy and stability must still be evaluated for the clinical environment.

Our results indicate that tablet computer based AR applications to treatment aspects of radiotherapy could be feasible with the existing technology. Our results also suggest that self-tracking, camera pose, and virtual content pose and representation could be improved by a reasonable amount, possibly through software corrections based on device-specific calibration of the tracking components. The HoloLens version on the other hand makes available a level of precision not yet adequate to applications to patient setup, with the exception of detecting large setup errors. This is confirmed by the following discussion about the patient setup experiment.

4.4 Experimental Evaluation of RAD-AR as a Tool for Treatment Patient Setup

4.4.1 Materials and Methods

The experimental goal was to estimate the precision of a patient set-up procedure based on the RAD-AR software only, without using the LINAC laser positioning system or the LINAC imaging devices.

For practical convenience we used the RANDO phantom as a substitute for a true patient. This represents a simplification of the problem, as the RANDO is a rigid object while a patient's body shape is only partly reproducible with the help of immobilization devices and has a degree of variability between the planning CT scan session and the treatment sessions. Implications of this aspect will be discussed below.

The RANDO was positioned with its vertical axis (intersection of the sagittal and frontal planes) perpendicular to the treatment couch. The cylinder marker was positioned on a stable support sufficiently close to the treatment couch to allow the experimenter to simultaneously see on the iPad screen the marker and the physical phantom from different viewpoints. The marker's support was also not too close to the couch, allowing couch linear motion of at least 8 cm in all directions and rotations of at least 5°.

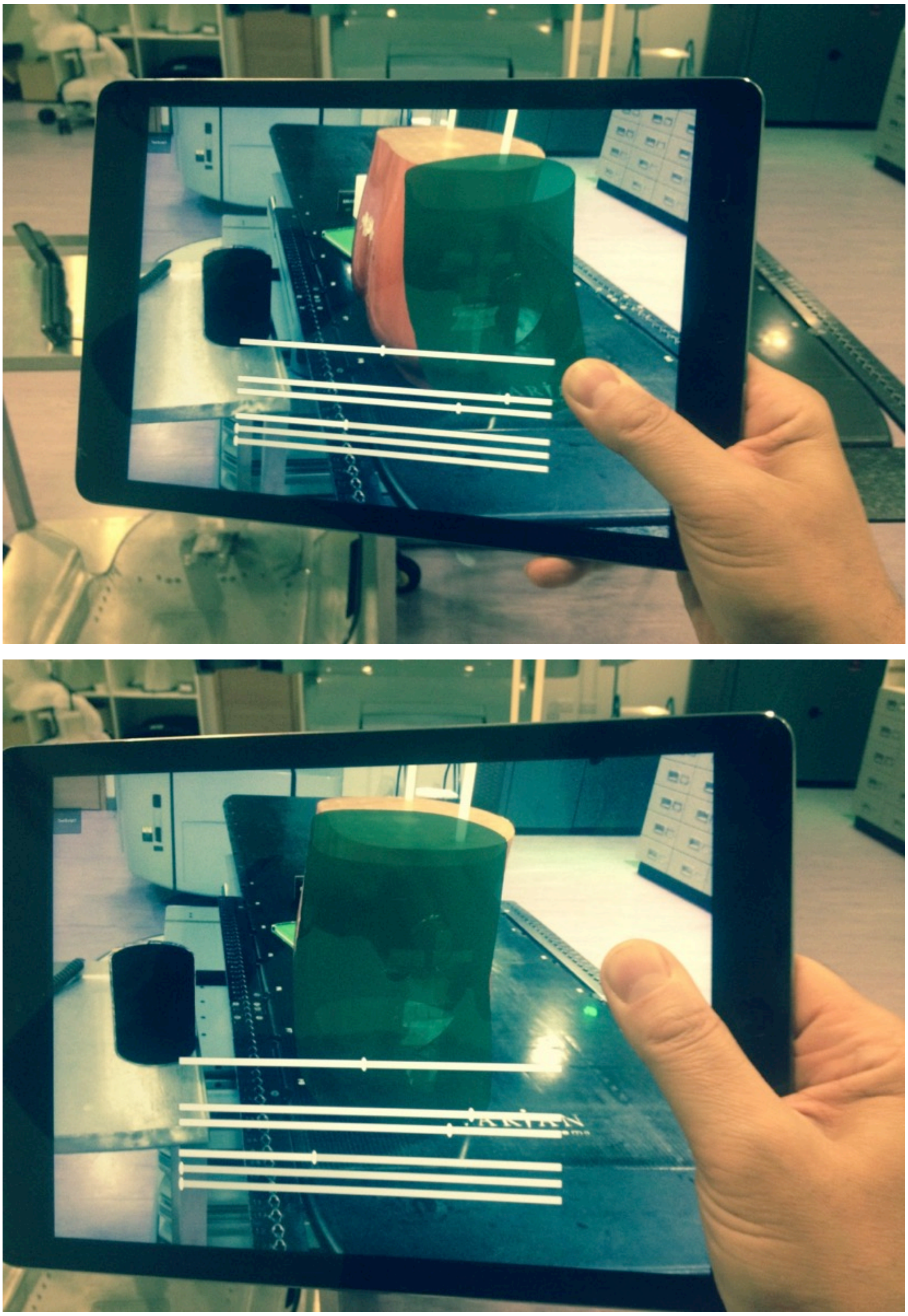


Figure 41 View through the iPad screen of both the physical RANDO phantom and AR rendering of its surface extracted from CT scan. The RANDO sits in a fixed position on the LINAC treatment couch. Horizontal, vertical, and lateral shifts, and rotation around the vertical axis are applied by the user to the couch using built-in motorized couch control to align the RANDO with its virtual model extracted from CT scan to evaluate reproducibility (i.e. precision) of final position.

The treatment couch used for this experiment has four degrees of freedom: vertical, lateral and longitudinal shifts controllable with a resolution of 1 mm, and rotation around the vertical axis passing through the isocentre with a 0.1° resolution.

Using the app's slider controls the AR RANDO body outline was overlaid onto the physical RANDO. The position of the AR body outline in physical space (as rendered on the tablet display) would ideally be fixed and independent from the tablet position and orientation; this position is the objective for the physical phantom position to be achieved using motorized couch shifts and rotation, using the app only. A shift of 5 cm in the three spatial direction and a rotation of 5° around the vertical axis through the machine isocentre was applied to the treatment couch where the RANDO was initially sitting aligned to the virtual outline. Looking at the scene through RAD-AR the physical mannequin was re-aligned with its virtual body outline and the values of couch longitudinal, lateral and vertical positions, and couch angle, were annotated. The procedure was repeated 20 times and the mean and standard deviation of couch longitudinal, lateral and vertical positions were calculated. The 20 measurements set was repeated 3 times. The standard deviations of measurements quantify the accuracy of a set-up procedure based on RAD-AR. The means represent the estimated setup position of the patient.

The procedure outlined above was repeated using the HoloLens, with the RANDO supine on the treatment couch.

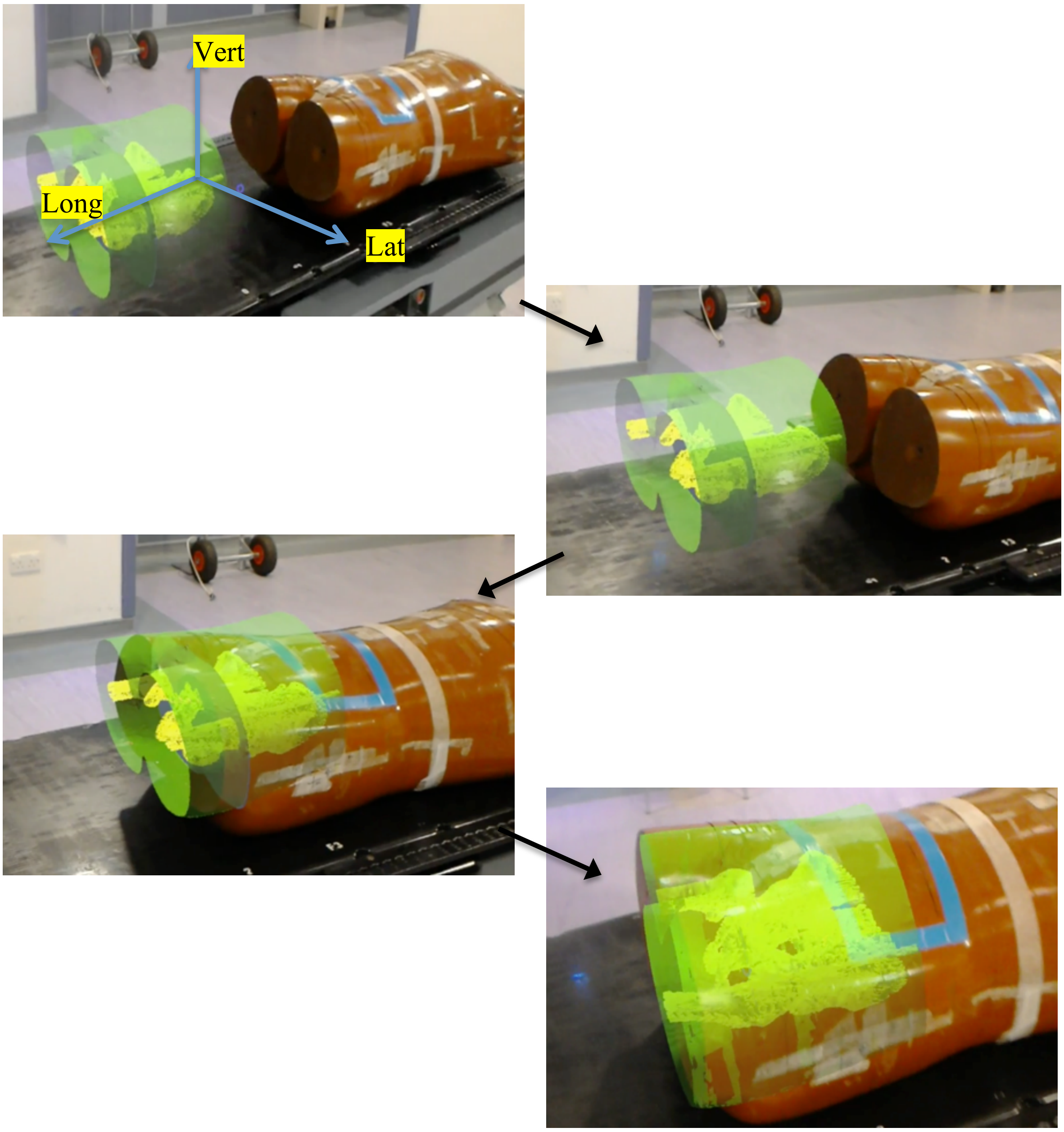


Figure 42 RANDO phantom sits in a fixed position on the LINAC treatment couch. Horizontal, vertical, and lateral shifts, and rotation around the vertical axis are applied by the user to the couch using built-in motorized couch control to align the RANDO with its virtual model extracted from CT scan to evaluate reproducibility (i.e. precision) of final position.

Figure 43 User wearing the HoloLens, controlling LINAC couch position to perform alignment of RANDO phantom with its virtual model extracted from CT scan to evaluate reproducibility (i.e. precision) of final position. Image in top left corner shows user view through the HoloLens.

4.4.2 Results

iPad

The average 3D vector magnitude of the error (an indicator of the quality of registration procedures used in radiotherapy, (Brock, 2014) p. 45) for the alignment of the physical RANDO mannequin with its AR body outline for the dataset was ±1.2 cm. Figure 44 shows a scatter plot of results for the first of the three sets of measurements. Table 2 shows mean of results for the three sets of measurements.

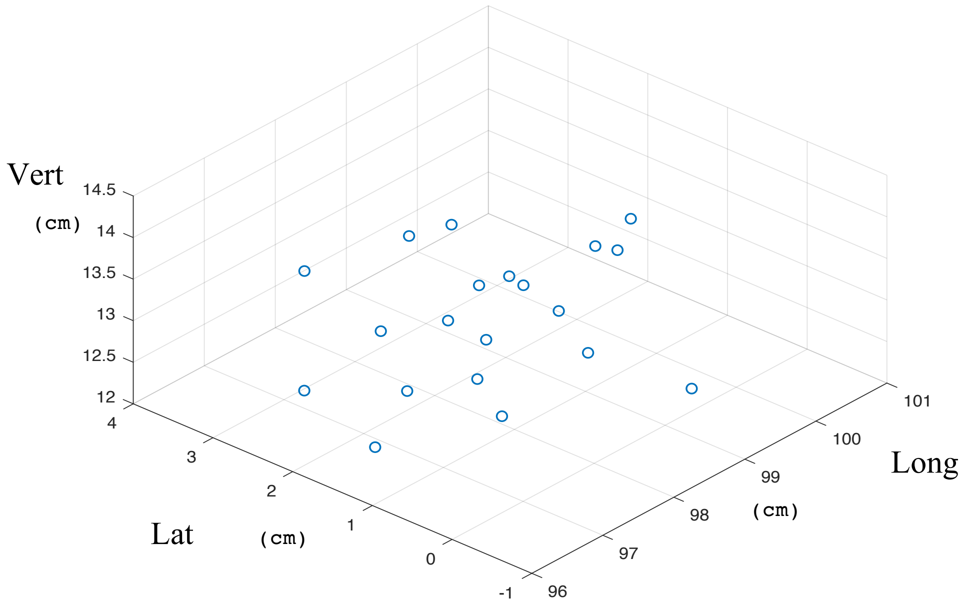


Figure 44 the first set of 20 measurements of couch positions (longitudinal, lateral and vertical) for the iPad version of RAD-AR.

Table 2 RANDO setup procedure using RAD-AR on the iPad: mean of final position of treatment couch for the three sets of 20 measurements.

	Measurements set 1	Measurements set 2	Measurements set 3
Mean:			
Long	98.3 cm	97.9 cm	98.2 cm
Lat	1.6 cm	1.3 cm	1.1 cm
Vert	13.0 cm	13.3 cm	13.1 cm
Couch angle	0.3°	0.6°	0.1°
Std Deviation			
Long	0.9 cm	0.7 cm	1.0 cm
Lat	0.7 cm	0.7 cm	0.8 cm
Vert	0.9 cm	0.6 cm	0.8 cm
Couch angle	1.3°	0.9°	1.0°

Measured precision of RANDO setup procedure using RAD-AR were:

- Longitudinal: 0.7 - 0.9 cm
- Lateral: 0.7 - 0.8 cm
- Vertical: 0.6 - 0.9 cm
- Couch angle: 0.9° - 1.3°.

Our results are of the same order of magnitude of results obtained in the only other similar study (but based on conventional monitor display) found in the literature (Talbot et al., 2009)

HoloLens

A similar set of measurements was performed for the HoloLens version of RAD-AR (Table 3).

Table 3 RANDO setup procedure using RAD-AR on the HoloLens: mean of final position of treatment couch for the three sets of 20 measurements.

	Measurements set 1	Measurements set 2	Measurements set 3
Mean: Long Lat Vert Couch angle	 98.2 cm 1.6 cm 12.4 cm 0.5°	 98.8 cm 0.3 cm 13.3 cm 0.5°	 98.0 cm -0.9 cm 13.3 cm 0.4°
Std Deviation: Long Lat Vert Couch angle	 1.5 cm 0.9 cm 0.9 cm 1.6°	 0.9 cm 1.2 cm 1.0 cm 1.2°	 1.4 cm 0.9 cm 1.2 cm 1.3°

Measured precision of RANDO setup procedure using RAD-AR was:

- Longitudinal: 0.9 - 1.5 cm
- Lateral: 0.9 - 1.2 cm
- Vertical: 0.9 - 1.2 cm
- Couch angle: 1.2° - 1.6°.

4.4.3 Discussion of Results

Precision of the iPad version of RAD-AR is in the range 0.7 - 0.9 cm and 0.9° - 1.3°, not yet adequate to patient setup. The HoloLens version performed slightly worse. Considering that the RANDO is a rigid object, results with a human patient would be expected to be worse than results obtained with the RANDO. Application to patient setup of our technology for patient setup is not likely with the existing technology. But despite this, RAD-AR, in its current state of development and in both the iPad and the HoloLens version, could be used to detect large setup errors (e.g. larger than 3 cm or 3°) arising from a number of other different causes, as described Yan et al. (Yan et al., 2013). A commercial system using surface image registration is considered by Krengli et al. (Krengli et al., 2009). Reported uncertainty is of the order of magnitude of our results with the iPad. The system (AlignRT system, Vision RT, London, UK) is based on highly specialized hardware; costs are of the order of $180,000 to $200,000, and the system is not open source or easily customizable by in-house software developers; this fact supports one of the claims made in our research hypothesis, i.e. that the development of clinical applications of AR in radiotherapy could benefit in terms of costs and portability if implemented on consumer electronics, as compared to existing commercial systems.

4.5 Detection of Patient Body Shape Change

4.5.1 Materials and Methods

As discussed in section 1.1.2, in order to accurately deliver a radiotherapy treatment, the patient body shape and the geometry of the internal anatomy should be as close as possible to those of the planning CT scan. In adaptive radiotherapy a CBCT scan of the patient can be acquired with the patient on the treatment couch prior, during, or after treatment, and compared with the planning scan. Acquisition of the CBCT scan implies a small radiation dose delivery to the patient. An alternative approach, not requiring extra dose delivery, has been considered here to acquire and compare the patient's body shape at treatment time with the planning CT scan. This technique has been investigated with the HoloLens version of RAD-AR, using the RANDO mannequin. A 3D model of the RANDO on the treatment couch was acquired using the Structure sensor (Occipital, San Francisco, CA, USA). The model was exported in

OBJ format and imported in RAD-AR using Unity. A shape change of the RANDO was physically simulated by using a treatment bolus sheet to enlarge the mannequin abdomen with two different thicknesses, 1 cm and 2 cm, and a 3D models were acquired with the Structure sensor. CT scans of the RANDO with 1 cm and 2 cm enlarged abdomen were also acquired, and 3D models of the body outline were extracted. Deformations of 1 cm and 2 cm were used as they cover the range of typical situations observed when a patient loses or gains weight; e.g. a CBCT is often requested when the abdomen diameter changes by at least 2 cm from planning scan to treatment.

Overlay of the planning CT scan body outline with the Structure models was attempted to investigate the potential of this technique to detect body shape changes.

4.5.2 Results

Comparison of the RANDO body outline extracted from the CT scan with models acquired using the Structure sensor allowed to detect an abdominal enlargement or reduction of 2 cm with high level of confidence; changes of 1 cm were not detectable with acceptable confidence.

Comparison of the physical RANDO body outline with models acquired with the Structure sensor allowed to detect 2 cm enlargement or reduction with high level of confidence; 1 cm changes were detectable with some uncertainty.

Comparison of the physical RANDO body outline with models extracted from the CT scan allowed to detect 2 cm enlargement or reduction with high level of confidence; 1 cm changes were not detectable with acceptable confidence.

4.5.3 Discussion of Results

Simulated patient body shape changes of 2 cm or more were detectable using the CT scan and the model acquired with the Structure sensor, suggesting that this technology has some potential for clinical applications, complementing, and possibly reducing the use of more invasive techniques (like e.g. acquisition of CBCT, involving radiation dose delivery). Since the RANDO is a rigid object, results with a human patient would be different, and would need further investigation, but the order of magnitude of detectable body shape changes could expected to be similar to what we achieved with the RANDO, as e.g. an abdomen expansion (or contraction) of a real patient, if the patient gains (or loses) weight, would affect a portion of the body surface of the order of several centimetres, and the experience with the HoloLens shows that this type of deformation can be detected.

Chapter 5. Patient Information Tool for Radiotherapy Practitioners

5.1 Importance of Correct Pre-treatment Preparation

As explained in section 1.1.2, at treatment time the internal anatomical conditions of the patient should be as close as possible to conditions when the CT scan was acquired. Consider the case of a patient undergoing radiotherapy treatment for prostate cancer. The prostate sits between the bladder and the rectum: the bladder and rectum conditions determine the position of the prostate, and the bladder conditions also affect the bowel position. Rectum (Takemoto et al., 2012) and bowel (Michaelson et al., 2008) (and other organs and tissues (Emami et al., 1991)) can suffer severe side effects if irradiated above a certain dose limit. Rectum and bladder conditions can be controlled by emptying the bladder or drinking water, and emptying the rectum with the help of enemas.

The most suitable and easily reproducible conditions are:

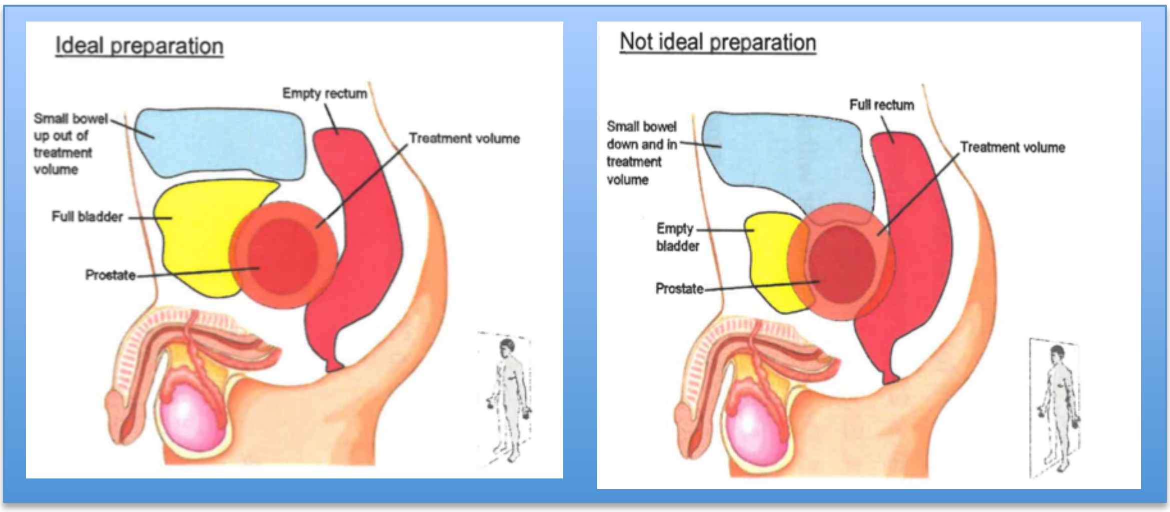
- full bladder (the amount of bladder included in to the treatment area is reduced), achieved by drinking a given amount of water at given times prior to each treatment fraction. It is the most suitable for treatment by external beam radiotherapy and it is also reproducible with acceptable accuracy;
- empty rectum (the rectum “collapses” away from the treatment area), achieved by enema.

Before starting radiotherapy the patient is explained its treatment by a radiotherapy practitioner, including the importance of reproducing at treatment time the planning scan anatomical position and internal physiological conditions (bladder filling and rectum evacuation). The practitioner role is very delicate; it involves dealing with patients from all cultural backgrounds and has important psychological implications (Halkett et al., 2016). The patient is given instructions to follow in preparation for treatment. Patient information is routinely delivered using drawings showing the patient’s internal anatomy and the way changes of anatomical conditions can affect the treatment outcome producing unwanted, often severe, side effects and reducing treatment effectiveness. Figure 45 and Figure 46 show a typical educational leaflet with instructions and illustrative drawings used by radiotherapy practitioners to explain to patients the changes that can occur in their internal anatomy in relation to preparation before treatment (bladder filling, rectum evacuation).

Treatment preparation

1. Arrive and check in at reception
2. Go into the toilet and use the enema
3. Wait for the enema to work - may take up to 20 minutes to work, try after 20 minutes and proceed to point 4
4. Empty bladder
5. Drink 500 ml water within 5 minutes
6. Wait …………………
7. Wait to be called for treatment, do not empty bladder
8. Change into dressing gown and slippers - leave underwear and t-shirt on

Figure 45 Example of educational leaflet reporting treatment preparation instructions for patients.



(a) **(b)**

Figure 46 Example of educational leaflet with illustrative drawings used by radiotherapy practitioners to explain patients changes in internal anatomy in relation to preparation before treatment. (a) Correct preparation full bladder, empty rectum; rectum and bowel intersection with treatment volume is limited. (b) Incorrect preparation empty bladder, full rectum; a significant amount of rectum and bowel falls inside the planned treatment volume.

5.2 Experimental Evaluation

5.2.1 Materials and Methods

We have implemented in RAD-AR a visualization tool for use by radiotherapy practitioners to explain to patients why it is important to follow correct pre-treatment preparation. In actual clinical use the practitioner and the patient will both wear the HoloLens, sharing the view of an AR scene showing a 3D model of the relevant patient anatomy and a representation of a treatment beam conforming to the PTV (prostate). At this stage, having only one HoloLens available for testing, the system it is only being evaluated by one of the users - the practitioner. With only one HoloLens available, this test could also have been done with a patient wearing the HoloLens and the practitioner using the computer monitor to see the scene. This was not done for lack of time to deal with ethical approval, as the HoloLens had become available at a late stage of the PhD research period. The shared AR experience will be considered for future work.

Two situations are presented to the user:

- one representing the configuration in Figure 46 (a), where correct preparation procedures were followed according to the instructions in Figure 45;
- one representing the configuration in Figure 46 (b), where correct preparation procedures according to the instructions in Figure 45 were not followed.

The AR content is overlaid to the physical RANDO mannequin to create a more realistic AR experience (Figure 47 and Figure 48). The users can move around the model and in clinical use the practitioner would point out to the patient the fact that the conformal radiation beam was based on the planning scan acquired in ideal conditions (full bladder, empty rectum), irradiating the cancer and sparing sensitive organs keeping the dose delivered to those below clinically relevant thresholds delimiting the onset of severe side issues (rectum/bowel bleeding, etc.). If the configuration is not reproduced when the treatment is delivered the internal anatomy can drastically change with the detrimental effect that the treatment beam can miss the target (prostate) and irradiate sensitive healthy organs above tolerated dose, making the treatment ineffective and producing severe side effects.

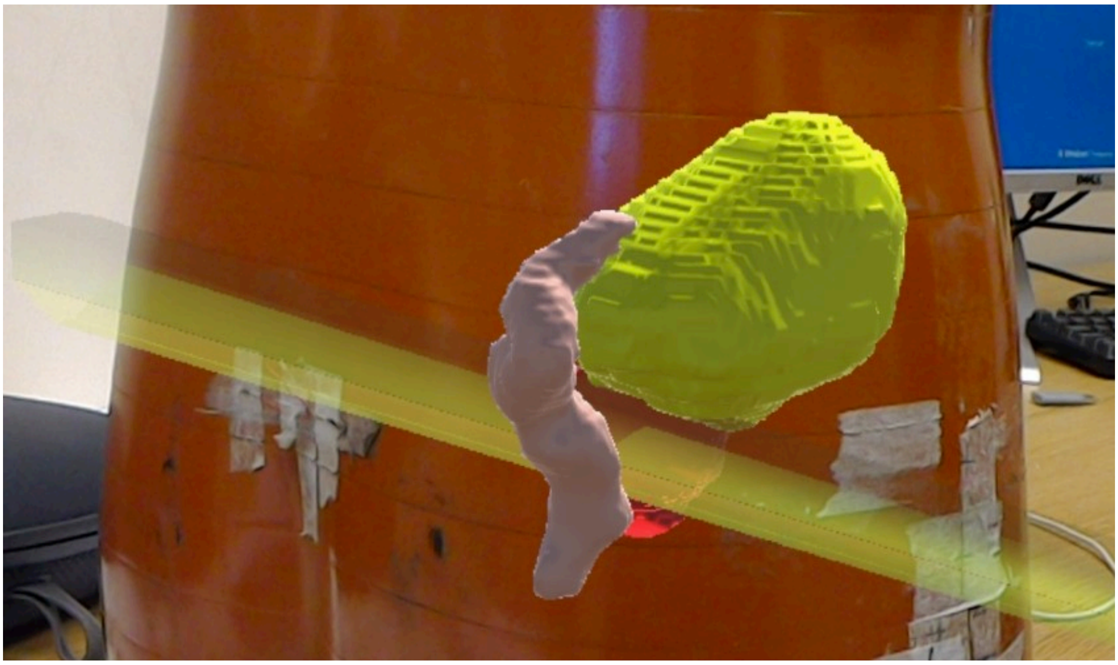


Figure 47 RAD-AR education tool. Correct bowel (empty) and bladder (full) preparation. Radiation beams hits the prostate (red), sparing rectum (grey) and bladder (yellow).

Figure 48 RAD-AR education tool. Incorrect bowel (full) and bladder (empty) preparation. Radiation beam partly misses the prostate (red), and hits part of the rectum (grey). Full rectum and empty bladder allowed the prostate to move anteriorly.

A user feedback study was carried out; 9 radiographers and 2 medical physicists where asked to evaluate the tool and complete the user feedback questionnaire in Figure 49. Although the sample size is not large enough to produce and statistical significance, the results will provide an indicator of the potential of AR as a patient education tool.

User feedback questionnaire

On the following scale:

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

how would you rate the following statements:

1. The AR system is easy to use.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

2. The leaflet based patient training system works better than the AR system.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

3. AR technology will be a regular part of patient training tools within the next 5 years.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

4. The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

5. A combination of leaflet based training and AR technology would be an optimum solution.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

6. The quality of the leaflet based representation is higher than the HoloLens representation of organs and treatment beams.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

7. The Microsoft HoloLens was comfortable wear.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

8. It is difficult to see the graphical visualization through the HoloLens visor.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

9. It would be better to view the information on a computer desktop monitor.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

10. Hand gestures in the AR system are intuitive and easy to use.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

Figure 49 Likert scale (Likert, 1932) **based user feedback questionnaire for RAD-AR patient education tool.**

5.2.2 Results

Likert [82] items are used to measure respondents attitudes to statement about the quality of the AR tool and how it compares to the leaflet. Whether a Likert scale can be considered as interval-level scale or as ordinal scale data is the subject of disagreement in the literature [141][142]. The ordinal interpretation is certainly correct; for Likert-type data a meaningful way to present results is using histograms.

The user feedback questionnaire was designed to reduce bias in the way questions are asked, towards either the HoloLens or the leaflet, by balancing the number of questions with positive emphasis on either the HoloLens or the leaflet.

Histograms corresponding to the 10 statements presented to users are shown in Figure 50 to Figure 59. Mean values make sense if we assume a degree of linearity in the (unknown) quantitative scale, and are shown in Table 5 (numeric values attributed to each judgement as shown in Table 4).

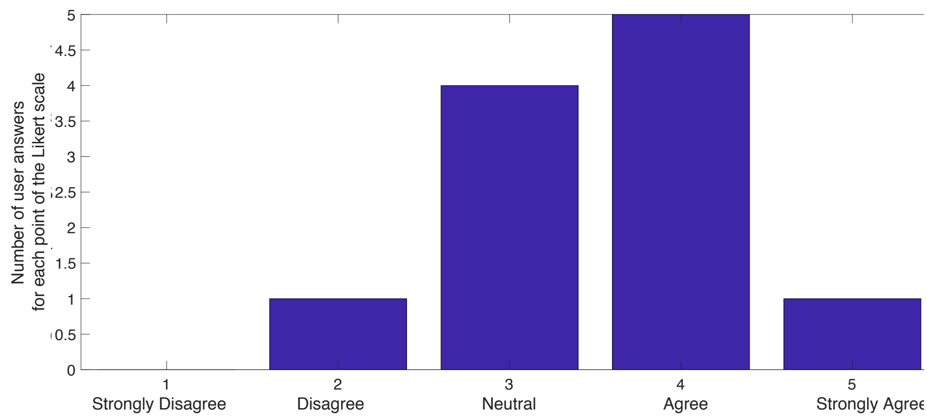


Figure 50 Statement 1: The AR system is easy to use.

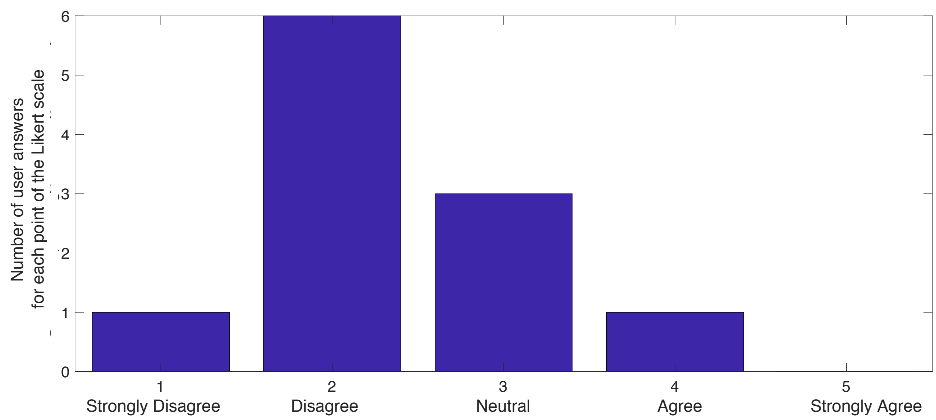


Figure 51 Statement 2: The leaflet based patient training system works better than the AR system.

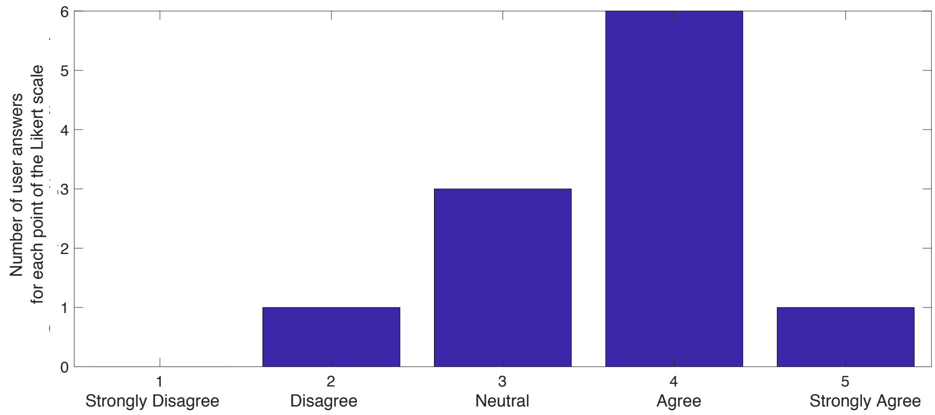


Figure 52 Statement 3: AR technology will be a regular part of patient training tools within the next 5 years.

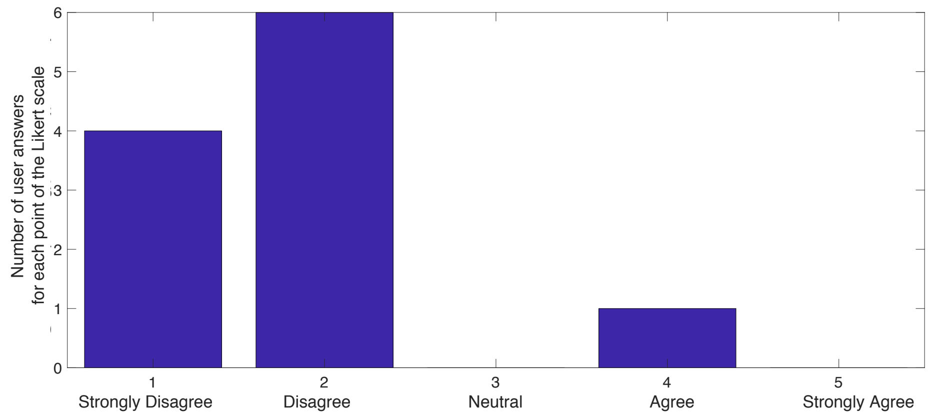


Figure 53 Statement 4: The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.

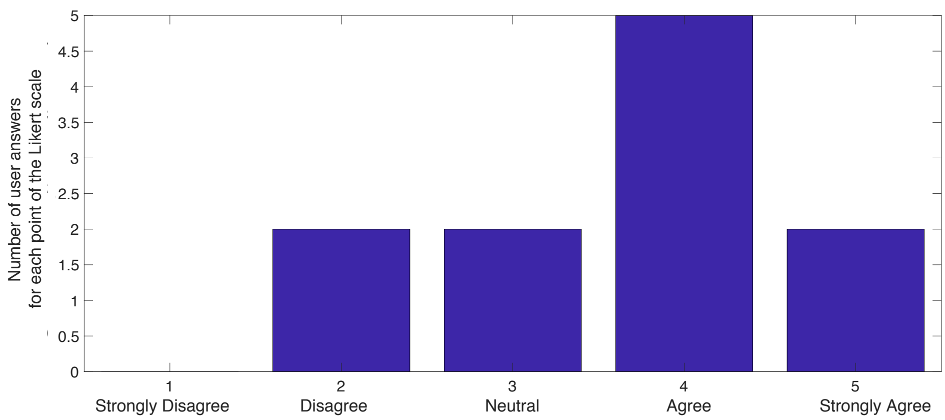


Figure 54 Statement 5: A combination of leaflet based training and AR technology would be an optimum solution.

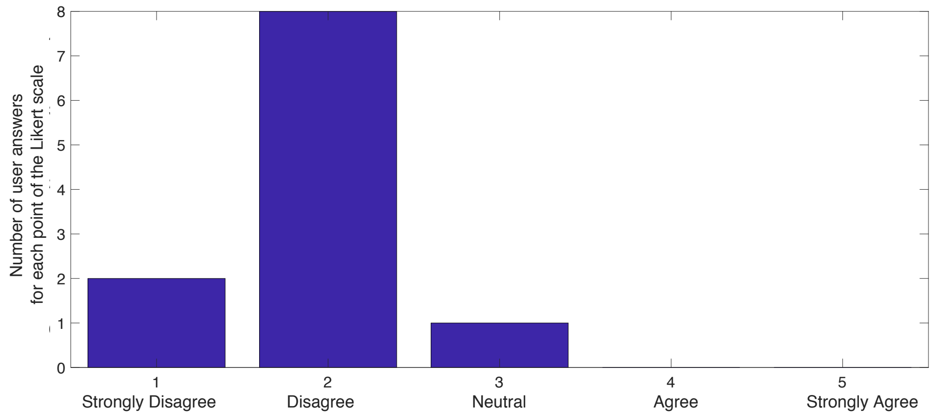


Figure 55 Statement 6: The quality of the leaflet based representation is higher than the HoloLens representation of organs and treatment beams.

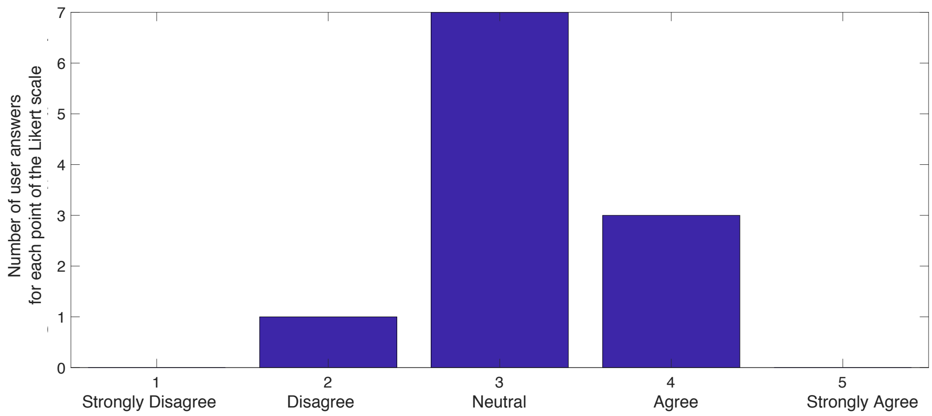


Figure 56 Statement 7: The Microsoft HoloLens was comfortable wear.

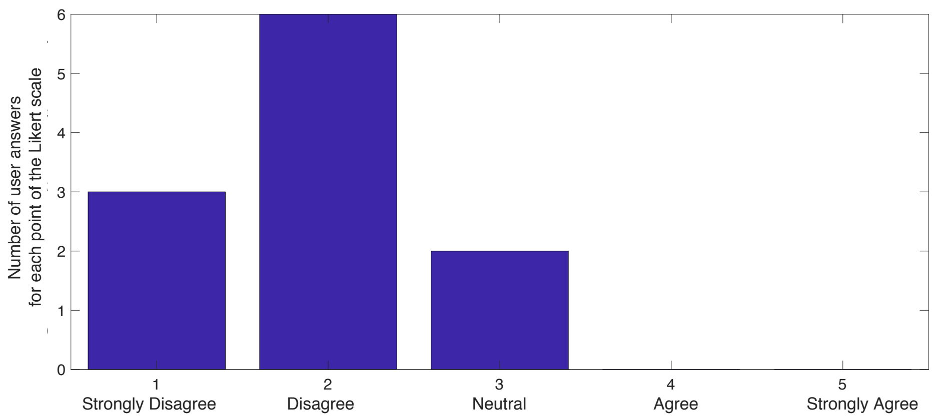


Figure 57 Statement 8: It is difficult to see the graphical visualization through the HoloLens visor.

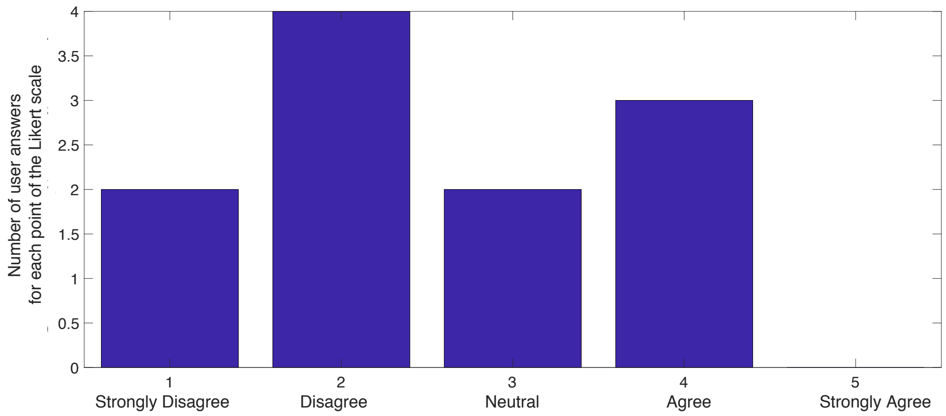


Figure 58 Statement 9: It would be better to view the information on a computer desktop monitor.

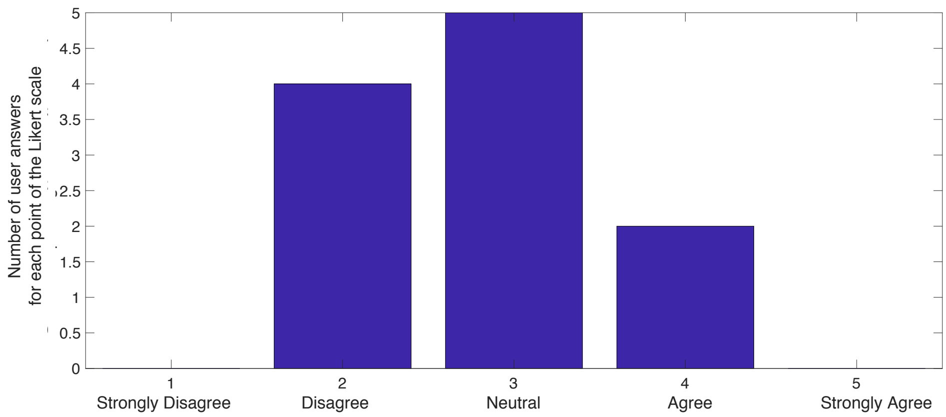


Figure 59 Statement 10: Hand gestures in the AR system are intuitive and easy to use.

Table 4 Numeric values attributed to Likert values to calculate average scores.

Answer	**Likert ordinal value**
Strongly Disagree	1
Disagree	2
Neutral	3
Agree	4
Strongly Agree	5

Table 5 Average Likert score for statements in user feedback questionnaire.

Statement	Average Likert score
1. The AR system is easy to use.	3.5
2. The leaflet based patient training system works better than the AR system.	2.4
3. AR technology will be a regular part of patient training tools within the next 5 years.	3.6
4. The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.	1.8
5. A combination of leaflet based training and AR technology would be an optimum solution.	3.6
6. The quality of the leaflet-based representation is higher than the HoloLens representation of organs and treatment beams.	1.9
7. The Microsoft HoloLens was comfortable wear.	3.2
8. It is difficult to see the graphical visualization through the HoloLens visor.	1.9
9. It would be better to view the information on a computer desktop monitor.	2.5
10. Hand gestures in the AR system are intuitive and easy to use.	2.8

5.3 Discussion of Results

Our results indicate an overall positive user evaluation (Table 5, average score higher than 3 = neutral) of the AR tool and are consistent with results of similar experiments conducted using VR technology (Sul e-Suso et al., 2015). Comfort and ease of use of the HoloLens was rated as neutral. Ease of visualization and quality of graphics content was considered positively; the graphical representation of radiotherapy concepts in AR was rated superior to the corresponding leaflet version. Patient education information is not presented on a computer desktop monitor at the NWCTC, but this is the case in other centres. This option was addressed in question 9; also in this case results suggest a user preference for the AR system. The size of the sample of users is not large enough to draw definitive conclusions (Park & Jung, 2009), but a clear interest and appreciation for the AR tool emerged.

There were other comments from the participants not captured in the questionnaire. The field of view in the HoloLens was considered too narrow; this is a well known problem ("This is how Microsoft's HoloLens will address its biggest flaw," 2017), and will likely be addressed in new versions of the device ("Microsoft Has Figured Out How to Double Field of View," 2017)("Microsoft Flat Lens Patent," 2017a). Usability can be improved by using vocal controls instead of hand gestures, and further improvements can be expected when the next generation of the HoloLens will be released.

Amongst other comments, one was particularly interesting; the idea that, if the hardware becomes lighter and the field of view increases in future versions of the device, as it is likely, using an AR tool instead of a diagram on paper to explain internal anatomy and details of their treatment to patients, would benefit elder patients especially, as they often struggle to understand pictures like Figure 46. Possibly, an AR render in 3D of the same information, overlaid to a physical mannequin, would be more naturally understood by the patient. On the HoloLens, as the visualization of 3D content was evaluated as satisfactory, the deployment of an AR patient education tool is something that we consider useful and already feasible with current technology, although implementation would be not optimal, due to limitations in the field of view and physical dimensions and weight of the hardware. A patient education tool implemented on the HoloLens (or any HMD available on the market) would be implemented on pairs of devices to be used at the same time by the radiotherapy practitioner, explaining the treatment and controlling the display of AR content, e.g. switching between display of internal anatomy corresponding to correct and incorrect bowel/bladder preparation, switching on/off display of treatment volumes and OAR outlines, as the verbal explanation of the treatment proceeds. It is our view that AR would contribute to reduce the gap between professionals with anatomy and medical background and patients with all possible backgrounds and ages, when the radiotherapy treatment is explained to the patient. Many patients know nothing about radiotherapy and very little about internal anatomy. Any improvement in understanding their treatment would be highly beneficial, as it is expected to increases the chances that correct pre-treatment preparation and during-treatment behaviour is followed, and correct treatment delivery is obtained (Graf, Boehmer, Nadobny, Budach, & Wust, 2012). Compared to the VR system considered in (Sul e-Suso et al., 2015) and (Williams et al., 2017) an AR tool implemented on the HoloLens would have advantages in terms of cost and logistics, as it could be used in any consultation room and several units could be easily made available (the system used in (Sul e-Suso et al., 2015) and (Williams et al., 2017) is based on expensive highly specialised hardware and needs a dedicated VR room to install large VR displays), and user experience ((Lok et al., 2003)(Kaufmann, 2003) see the discussion on potential advantages of AR over VR, section 1.2).

Chapter 6. Visualization aid for Clinicians

6.1 Treatment Plan Evaluation Process

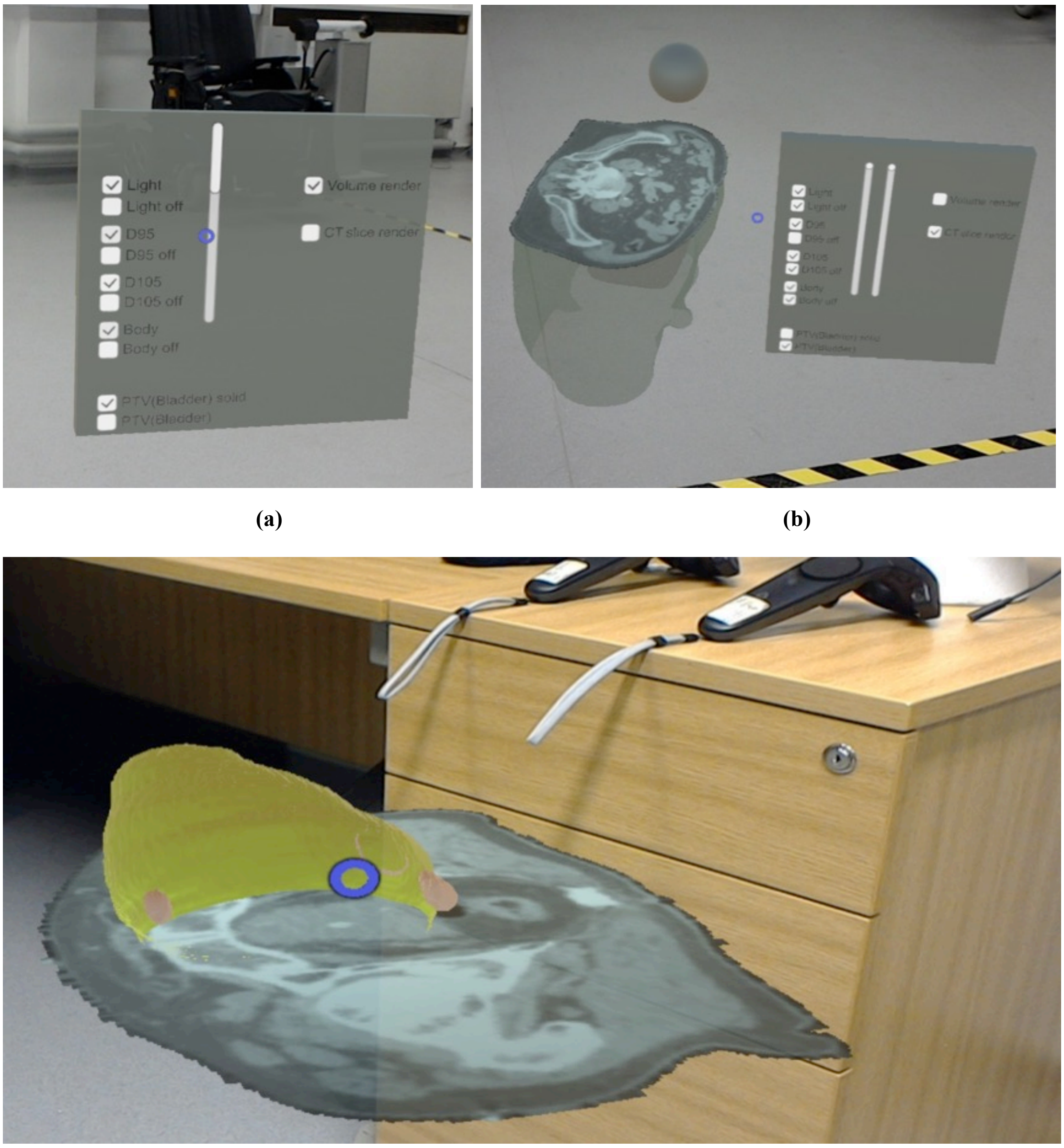
Visualization and evaluation of radiotherapy treatment plans is routinely carried out on computer workstation displays or tablet computers (Hahn, Shalev, & Therrien, 1987). A number of alternative approaches, and benefits and drawbacks were discussed in chapter 2.

The clinician evaluates dose coverage of the PTV and the dose received by organs at risk. Evaluation of PTV coverage includes a slice-by-slice inspection of inclusion of the PTV by the clinically relevant 95% isodose curve; this corresponds in 3D to inclusion of the PTV 3D surface inside the 95% isodose 3D surface. Coverage is usually not full and quantitative measures are also used (e.g. dose histograms (Khan, 2014)), but visual inspection by the clinician remains one of the main elements to decide treatment approval.

6.2 Experimental Evaluation

6.2.1 Materials and Methods

We implemented in RAD-AR a tool that allows visualization of isodose surfaces and PTV with semi-transparent and solid rendering for a bladder cancer conformal treatment plan with 4 static fields. CT slices were rendered as AR content registered in 3D with the PTV and isodose outlines; a slider control was implemented to allow the user to scroll through different CT slices (Figure 60).



(a) (b)

(c)

Figure 60 RAD-AR for plan evaluation. (a) User controls to switch on/off display of AR elements (light, isodose surfaces, PTV), scroll through CT slices. (b) User controls and patient body outline with scrollable CT slice. (c) RAD-AR rendering of a CT slice and PTV (bladder) surface.

A rudimentary method producing volume rendering effects was used to render semi-transparent sections of the CT dataset corresponding to transverse CT slices covering segments of the vertical axis (intersection of the sagittal and frontal planes) of 3 cm length (Figure 60). A hand-draggable light source AR object was used to provide a tool to change contrast/luminosity of regions of the CT dataset; this avoids writing complex image processing code for the HoloLens (to satisfy the meta-requirement that no low level coding should be required).

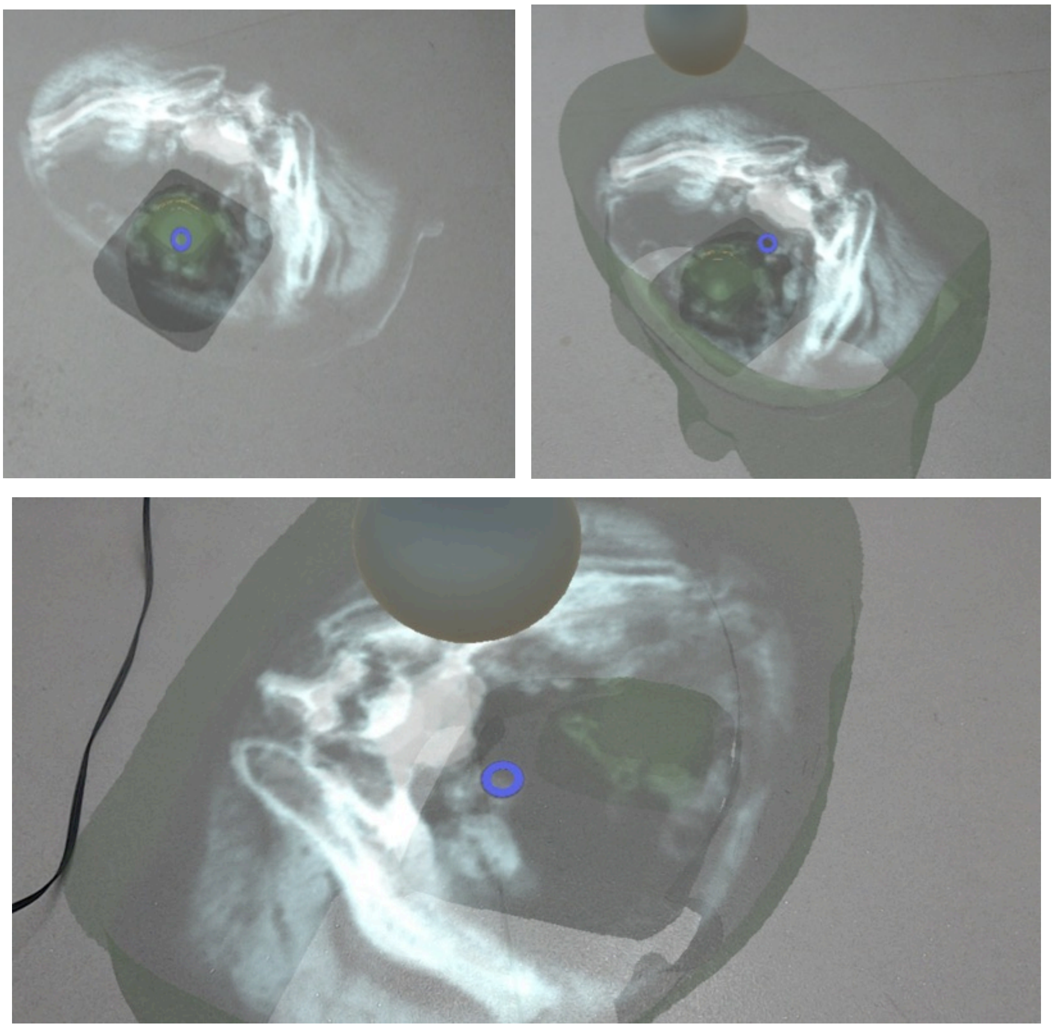


Figure 61 Rudimentary technique to produce volume rendering effects by render semi-transparent rendering of sections of the CT dataset corresponding to transverse CT slices covering segments of the vertical axis of 3 cm length. Isodose surface for 95% of prescribed dose and PTV outline is also rendered. The sphere is a hand-draggable light source used to provide some control over luminosity and contrast of the CT dataset rendering.

We carried out an experimental evaluation by asking two radiation oncologists and three medical physicists of the NWCTC to test the system. A conventional conformal 4 static fields bladder treatment plan was evaluated using RAD-AR. The clinicians assessed the 95% prescribed dose coverage (regions where the delivered dose exceeds the clinically effective value of 95% of the prescribed dose (Khan, 2014)) of the PTV and dose hotspots (regions where the delivered dose exceeds 105% of the prescribed dose) location and geometry. RAD-AR can easily visualize isodose surfaces and radiotherapy structures like the PTV, rendered with different levels of transparency and in different colours (Figure 62).

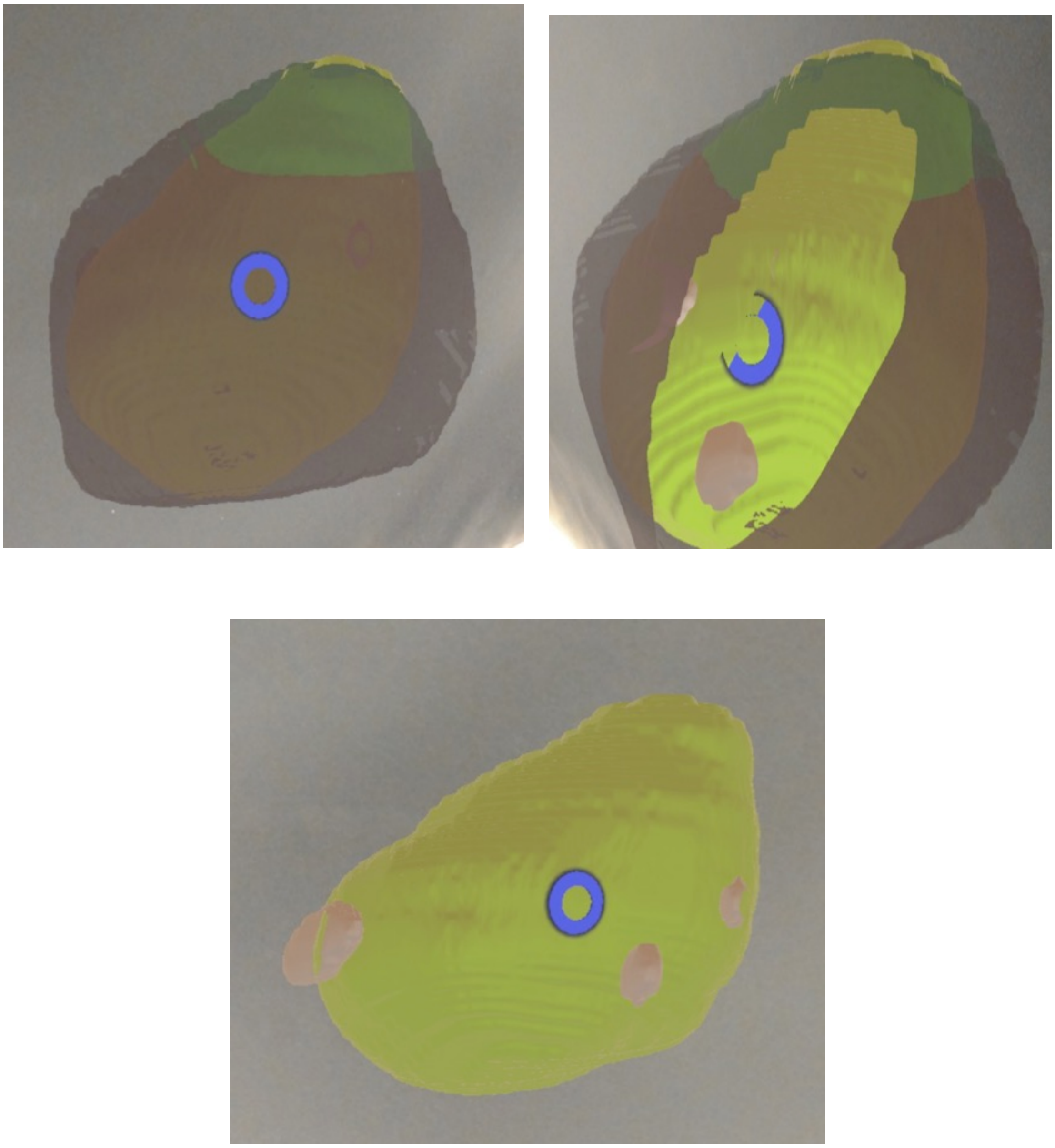


Figure 62 AR rendering on the HoloLens of 95% isodose surface (brown), PTV (prostate, yellow) and 105% isodose surface (pink). The blue ring is the HoloLens gazing cursor.

We asked the users to answer the questionnaire in Figure 63.

User feedback questionnaire

On the following scale:

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

how would you rate the following statements:

1. The AR system is easy to use.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

2. The 2D display based system allows a better understanding of the 95% dose coverage of PTV and 105% dose hotspots than the AR system.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

3. AR technology will be a regularly used in treatment planning within the next 5 years.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

4. The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

5. A combination of 2D display based and AR technology based plan evaluation would be an optimum solution.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

6. The quality of the 2D display based representation is higher than the HoloLens representation of PTV and isodose surfaces.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

7. The Microsoft HoloLens was comfortable wear.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

8. It is difficult to see the graphical visualization through the HoloLens visor.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

9. It would be better to view the information on a computer desktop monitor.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

10. Hand gestures in the AR system are intuitive and easy to use.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

Any other comments

____

____

Figure 63 Likert scale (Likert, 1932) **based user feedback questionnaire for RAD-AR plan evaluation tool.**

6.2.2 Results

The same preliminary considerations about interpretation of Likert scale data apply as explained in section 5.2.1.

Histograms corresponding to the 10 statements presented to users are shown in Figure 64 to Figure 73.

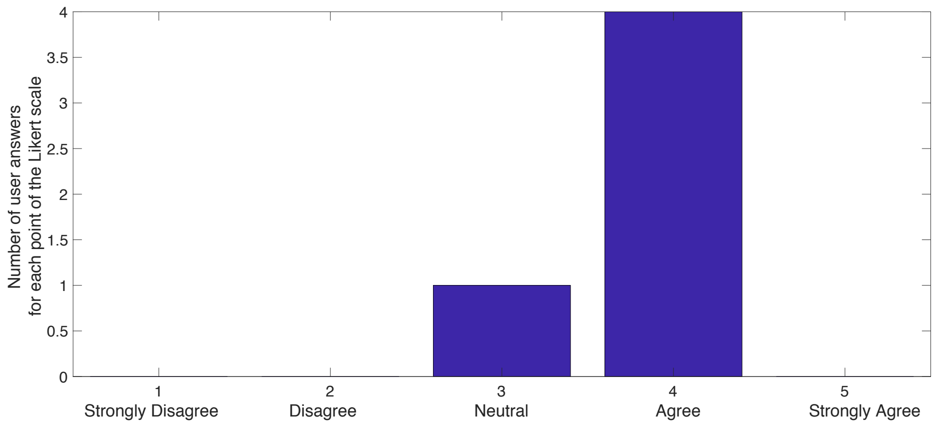


Figure 64 Statement 1: The AR system is easy to use.

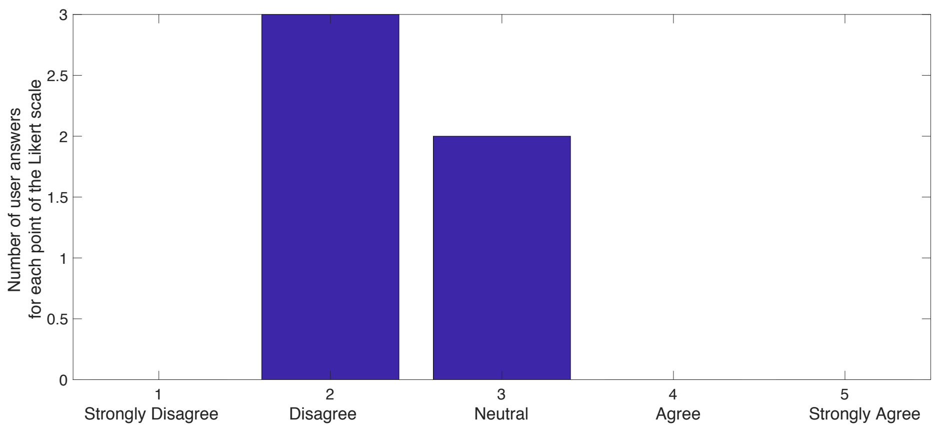


Figure 65 Statement 2: The 2D display based system allows a better understanding of the 95% dose coverage of PTV and 105% dose hotspots than the AR system.

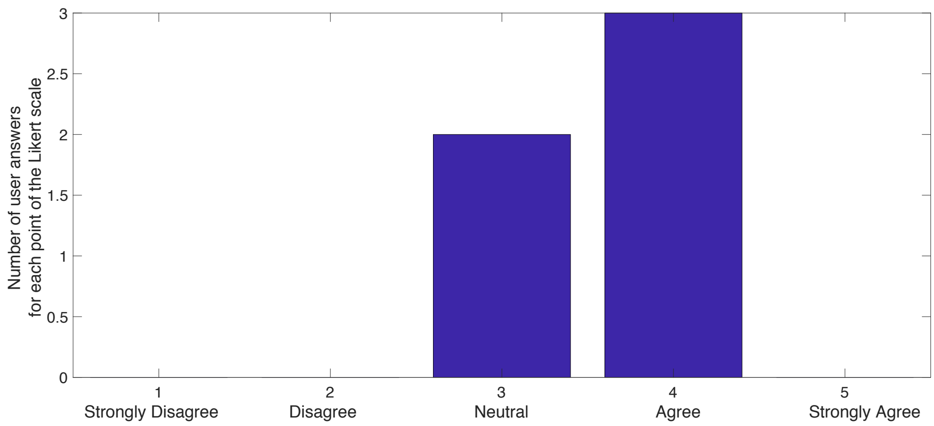


Figure 66 Statement 3: AR technology will be a regularly used in treatment planning within the next 5 years.

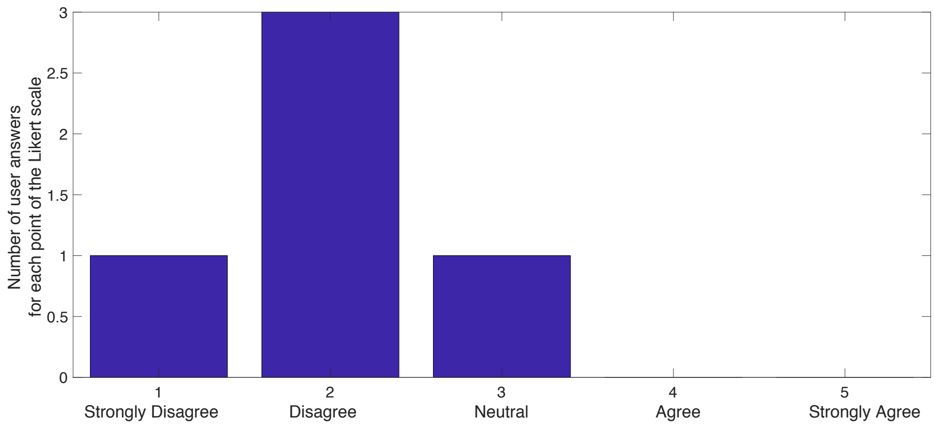


Figure 67 Statement 4: The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.

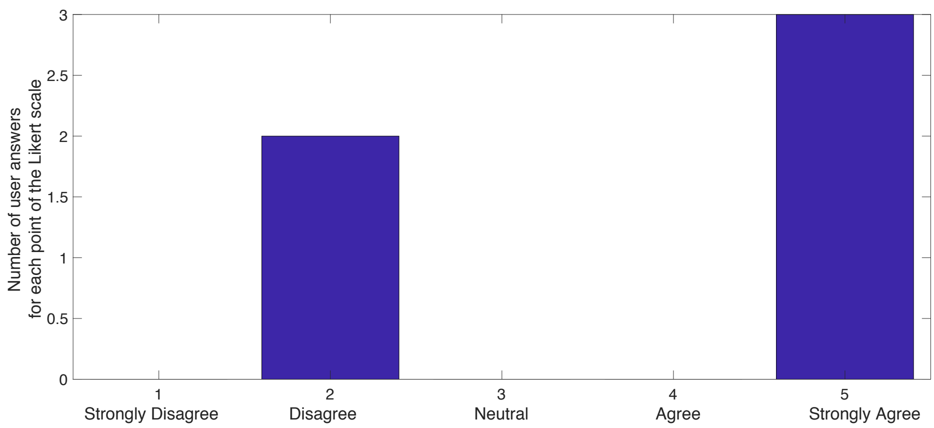


Figure 68 Statement 5: A combination of 2D display based and AR technology based plan evaluation would be an optimum solution.

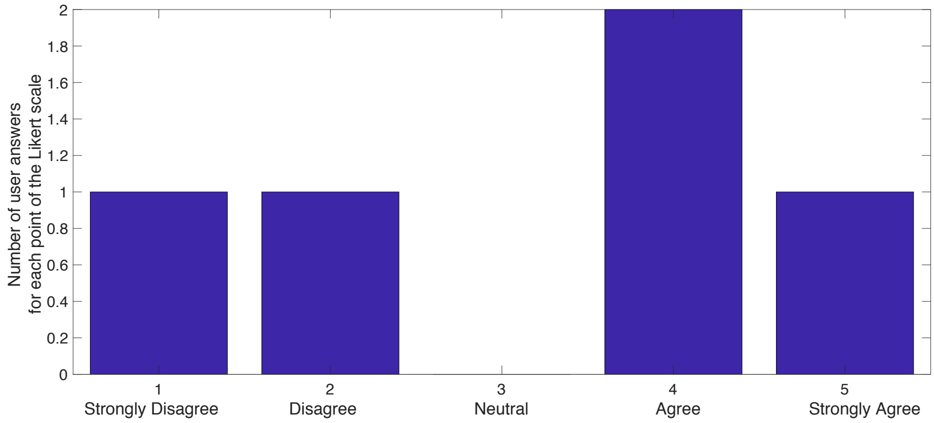


Figure 69 Statement 6: The quality of the 2D display based representation is higher than the HoloLens representation of PTV and isodose surfaces.

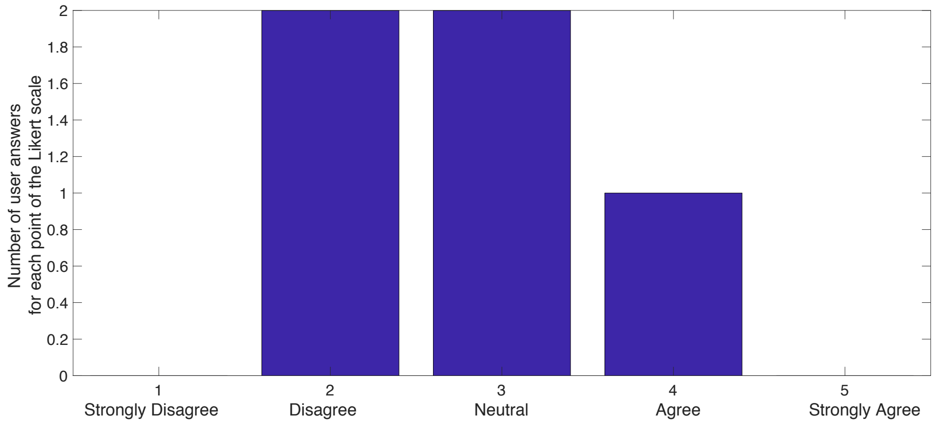


Figure 70 Statement 7: The Microsoft HoloLens was comfortable wear.

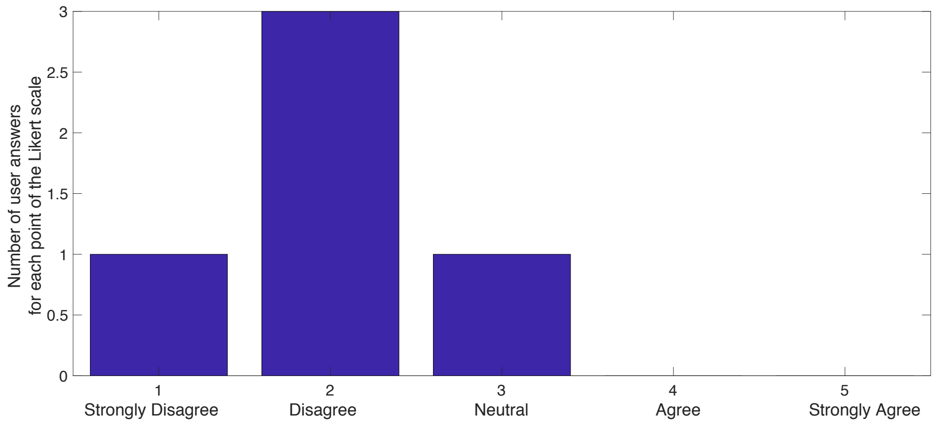


Figure 71 Statement 8: It is difficult to see the graphical visualization through the HoloLens visor.

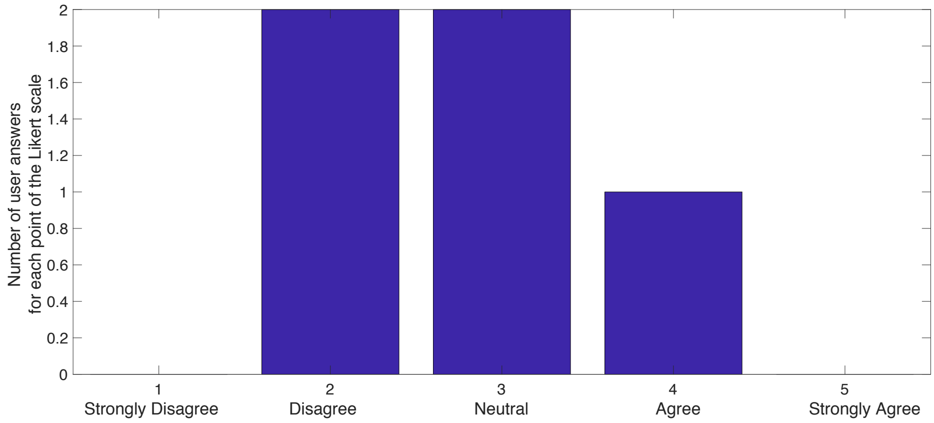


Figure 72 Statement 9: It would be better to view the information on a computer desktop monitor.

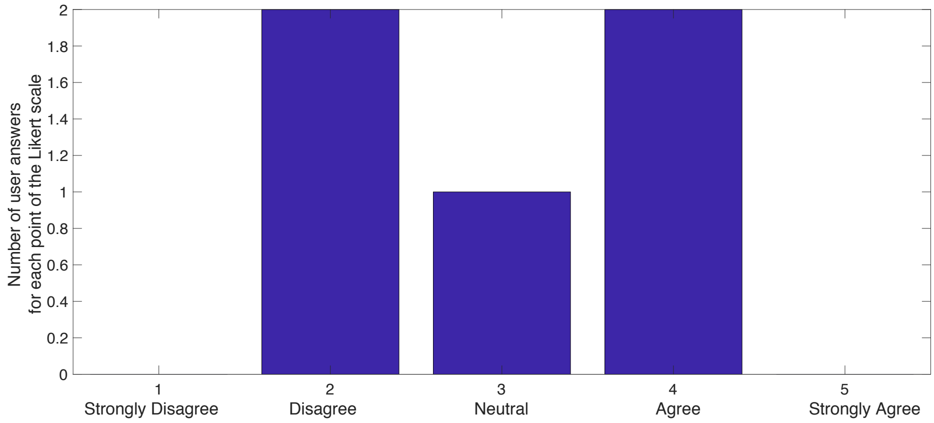


Figure 73 Statement 10: Hand gestures in the AR system are intuitive and easy to use.

Table 7 summarizes average Likert scores for each statement presented to users, for numeric values attributed to each judgement as shown in Table 4.

Table 6 Numeric values attributed to Likert values to calculate average scores.

Answer	**Likert ordinal value**
Strongly Disagree	1
Disagree	2
Neutral	3
Agree	4
Strongly Agree	5

Table 7 Average Likert score for statements in user feedback questionnaire for RAD-AR plan evaluation tool.

Statement	Average Likert score
1. The AR system is easy to use.	3.8
2. The 2D display based system allows a better understanding of the 95% dose coverage of PTV and 105% dose hotspots than the AR system.	2.4
3. AR technology will be a regularly used in treatment planning within the next 5 years.	3.6
4. The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.	2.0
5. A combination of 2D display based and AR technology based plan evaluation would be an optimum solution.	3.8
6. The quality of the 2D display based representation is higher than the HoloLens representation of PTV and isodose surfaces.	3.2
7. The Microsoft HoloLens was comfortable wear.	2.8
8. It is difficult to see the graphical visualization through the HoloLens visor.	2.0
9. It would be better to view the information on a computer desktop monitor.	2.8
10. Hand gestures in the AR system are intuitive and easy to use.	3.0

6.3 Discussion of Results

Overall user evaluation of the AR tool was positive. Figure 64 to Figure 73, and Table 7 show appreciation (score higher than 3 = neutral) of the features implemented in plan evaluation tool. Results for the plan evaluation tool are similar to results obtained for the patient education tool. Similarly to the patient education tool, comfort and ease of use of the HoloLens was rated as neutral, and ease of visual perception and quality of graphics content was considered positively. Similarly to what happened with the patient education tool, the field of view of the HoloLens was considered too narrow ("This is how Microsoft's HoloLens will address its biggest flaw," 2017); as pointed out in section 5.3 this issue will likely be addressed in new versions of the HoloLens ("Microsoft Has Figured Out How to Double Field of View," 2017).

The graphical representation of isodose surfaces and PTV was rated better on the AR tool compared to that of a 2D display for two users, and worse for three users. Considering that visualization of dose distributions and PTV is a task routinely carried out by planners and clinicians on 2D displays slice-by-slice several times every day, over several years of experience, a result not showing a clear preference of the 2D display over the AR tool needs to be seen in that context, i.e. as overall encouraging.

The size of the sample of users is too small to draw statistically meaningful final conclusions but a general appreciation of utility of AR applications to radiotherapy emerged. Comments from some users pointed out a possible positive effect in understanding complex cases, possibly using AR technology and visualization on 2D displays in a complementary way. Use of gaming controls for data navigation was suggested by one radiation oncologist; this would in fact be the solution preferred by the author to the data navigation problem, and will be considered amongst future developments. Commercial applications of RAD-AR were also suggested by the same clinician, e.g. as a tool to help understanding of CBCT data acquired at treatment time and comparison with planning CT data, exploiting multi-user interaction and intuitive perception of geometric features.

Clinicians also appreciated the possibility to increase the functionalities of RAD-AR to include several users to share a simultaneous view of the AR scene, while still seeing the real scene and other users, as this would allow to interact in a natural way with other radiotherapy professionals (e.g. by pointing at virtual objects, or physically seeing and talking to other users) to discuss and evaluate radiotherapy treatments. Natural multi-user interaction is in fact the main reason we think that AR is superior to VR for radiotherapy planning, and an in-depth study of this aspect will be the object of future developments ((Lok et al., 2003)(Kaufmann, 2003) see the discussion on potential advantages of AR over VR, section 1.2).

In a recent study (Mohiuddin et al., 2017) a radiotherapy plan visualization tool on the HoloLens was implemented a practical method was demonstrated for transition from indirect 2D visualization of the planned dose distribution using isodose lines to direct 3D evaluation of isodose volumes. Our system, RAD-AR, was developed, and results published, contemporarily to (Mohiuddin et al., 2017);

compared to (Mohiuddin et al., 2017) we have carried out quantitative investigation of accuracy, precision, and fidelity of content representation, not included in that study.

A comparison of data analysis techniques considering conventional and AR visualization based identification of fMRI features is discussed in (de Ridder et al., 2015). The authors point out that the visualisation currently relying on traditional 2D displays with WIMP interface limits the intuitive presentation of the data, and that VR/AR (using gesture-based inputs to create an immersive environment) for data visualisation can potentially allow a reduction in visual clutter a more natural data navigation. We believe that similar benefits would apply to AR applications to radiotherapy treatment planning.

Chapter 7. Conclusions and Future Work

Applications based on RAD-AR are able to display visual information extracted from patient's CT scans (e.g. organ outlines, CT slices, CT volume data) and radiotherapy plans (e.g. treatment beams, isodose surfaces, shielding devices) as augmented reality content. This is the first outcome of this research, showing feasibility of the project and laying the foundations for the development of future AR clinical tools for use in radiotherapy.

The functionalities specified in section 3.1 were all implemented. In order to evaluate applicability of RAD-AR to the treatment phase a quantitative testing was performed to estimate accuracy and precision of camera pose, precision of placement of virtual content in the real scene, faithfulness of visual geometric representation, sensitivity to detect anatomical changes of the patient, and precision of treatment setup.

Use of RAD-AR to implement a patient education and a plan evaluation tool was also investigated with two user feedback studies. The system was presented and demonstrated at two scientific conferences and received appreciation from the conference delegates (best poster award, (Cosentino et al., 2017)).

To analyse the results obtained we consider two types of potential benefits that could originate from clinical application of AR features implemented in RAD-AR:

- quantitative geometric aspects
- qualitative visualization aspects.

7.1.1 Quantitative Geometric Aspects

Accuracy and precision of camera pose were in the range of tolerances accepted in most radiotherapy procedures (e.g. 2 mm for treatment couch position for VMAT treatments, 1 mm to 2 mm for mechanical quality control tests on LINAC) for the iPad, and slightly above for the HoloLens. Precision and geometric fidelity of AR content rendering (0.2-0.3 cm) and precision of patient setup (0.7-0.9 cm) were close to the acceptable requirements for most radiotherapy procedures. The iPad could be applicable to patient setup, complementing current clinical practice methods, if an improvement of the order of 30% in self-tracking (from 0.2-0.3 cm to 0.1-0.2 cm) and 65% in patient setup precision (from 0.7-0.9 cm to 0.2-0.3 cm) could be achieved. This could possibly be obtained with software corrections or optics calibration. Improvements in the hardware specifications of new versions of the iPad will also impact the feasibility of clinical AR when released (speculation includes the iPad introducing a depth sensing camera in future releases (“This Apple iPhone X feature,” 2017), (“Apple iPad Pro 2018,” 2017)).

The HoloLens based patient setup tool needs major improvement in accuracy (about 80%, from 0.9-1.5 cm to 0.2-0.3 cm) before it could be considered for use in clinical practice. Virtual content placement and fidelity of reproduction for the HoloLens gave similar results to the iPad, with a smaller but still significant advantage for the iPad.

Although the iPad version performed significantly better than the HoloLens version in patient setup, the iPad version is marker based and, as already discussed, this imposes limitations to use with respect to the size and geometry of the space region where the self-tracking works. A possible solution would be to employ a multi-markers extension of the technique, but this approach would add an overall uncertainty and poses other technical problems such as co-registration of different markers (Yoon, Park, & Kim, 2006) (Wagner, Pintaric, Ledermann, & Schmalstieg, 2005).

The HoloLens version uses markerless self-tracking, but markerless camera pose is reported in the literature as less accurate than marker based camera pose (“Markerless inside-out tracking,” 2017) (Yang et al., 2008). An improvement in self-tracking for the HoloLens is to be expected, as the device used in our experiments is the first generation, and Microsoft appears to be committed to implement major improvements to the specifications in future releases (“Microsoft’s second-generation HoloLens,” 2017), (“Microsoft Flat Lens Patent,” 2017b).

The same type of considerations applies to potential applications for detection of patient body shape changes; in our opinion the HoloLens shows potential for clinical applications in the near future. Patient’s body changes of more than 2 cm could be detected with current technology.

We consider applications of RAD-AR on the HoloLens to detect large setup errors of more than 2 cm (e.g. a situation where LINAC couch shifts are applied in the wrong direction or magnitude at treatment time, or other situations described in (Yan et al., 2013)) feasible with current technology, subject to minor further experimental investigation, software robustness investigation, and clinical commissioning.

7.1.2 Qualitative Visualization Aspects

Two user feedback studies were carried out:

- evaluation of a patient information tool for radiotherapy practitioners, 11 users (9 radiographers and 2 medical physicists); and
- evaluation of a plan evaluation tool, 5 users (2 radiation oncologists and 3 medical physicists).

In both cases, users were asked to rate their opinions using a Likert scale questionnaire. The questionnaires used a similar structure for both studies. An overall appreciation and interest for applications of AR to radiotherapy patient education and treatment planning emerged. The two samples were not large enough to draw definitive conclusions but comparing results demonstrates a good agreement between all corresponding statements can be observed (Figure 74). The Spearman's rank correlation coefficient (a nonparametric measure of rank correlation of two variables, appropriate for ordinal data (Mukaka, 2012)) for the two series is 0.79; the two datasets can considered as a coherent set of statements about comparison of AR and 2D display visualization quality of RT concepts. The statement about visualization of dose distribution and PTV (n. 6 in the plan evaluation tool questionnaire) is the only one where preference was given to conventional 2D displays; it is also the only one where average ranking that does not agree with the corresponding statement in the patient education tool questionnaire. This can be understood considering that radiotherapy planners and clinicians are highly acquainted with use od 2D displays for those tasks; an initial training with the HoloLens would probably modify users ranking of statement 6 (in fact positive answers came from the two users that had the opportunity to test the system for a period of time longer than the other three users)

Summarizing, an overall appreciation of both the patient education tool and the plan evaluation tool emerged. The combined sample size of the two user feedback experiments (16 users answering rating 10 statements each, total of 160 data points) allows us to draw, if not statistically *definitive*, at least *meaningful* conclusions (Park & Jung, 2009) (McCrum-Gardner, 2010).

Table 8 Statements from user feedback questionnaires. Statements with same number have essentially the same meaning, adapted to the tool considered in the user feedback experiment.

Patient education tool	Plan evaluation tool
1. The AR system is easy to use.	The AR system is easy to use.
2. The leaflet based patient training system works better than the AR system.	The 2D display based system allows a better understanding of the 95% dose coverage of PTV and 105% dose hotspots than the AR system.
3. AR technology will be a regular part of patient training tools within the next 5 years.	AR technology will be a regularly used in treatment planning within the next 5 years.
4. The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.	The quality of the graphical representation of relevant radiotherapy concepts in the AR app is not acceptable enough.
5. A combination of leaflet based training and AR technology would be an optimum solution.	A combination of 2D display based and AR technology based plan evaluation would be an optimum solution.
6. The quality of the leaflet-based representation is higher than the HoloLens representation of organs and treatment beams.	The quality of the 2D display based representation is higher than the HoloLens representation of PTV and isodose surfaces.
7. The Microsoft HoloLens was comfortable wear.	The Microsoft HoloLens was comfortable wear.
8. It is difficult to see the graphical visualization through the HoloLens visor.	It is difficult to see the graphical visualization through the HoloLens visor.
9. It would be better to view the information on a computer desktop monitor.	It would be better to view the information on a computer desktop monitor.
10. Hand gestures in the AR system are intuitive and easy to use.	Hand gestures in the AR system are intuitive and easy to use.

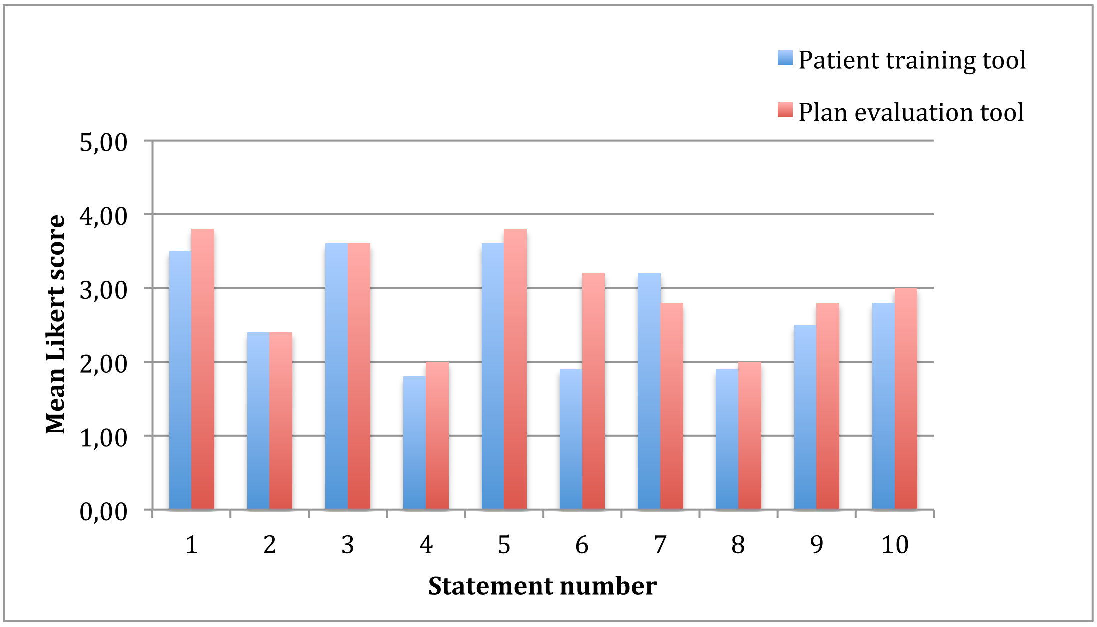


Figure 74 Mean Likert score (scale: strongly disagree = 1, disagree = 2, neutral= 3, agree = 4, strongly agree = 5) for corresponding statements of the user feedback tests of plan evaluation tool and patient education tool. Statements 1, 3, 7, and 10 are positive for the AR system. Statements 2, 4, 6, 8, and 9 are negative for the AR system. Statement 5 is positive about using a combination of 2D and AR visualization.

7.2 Discussion of Results

We consider the use of applications developed using RAD-AR as radiotherapy set-up tool not yet feasible with current technology; it could become a realistic option on the HoloLens if in the next generations of the device sufficient improvement (e.g. reducing camera pose errors by 60–70% from 0.7–1.0 cm to 0.2–0.3 cm) will be achieved for self-tracking. Although the iPad version performed better in all quantitative experiments, clinical applications of the iPad version are less likely to be expected, due to the marker based self-tracking technology imposing spatial constraints on usability. Correct positioning of any markers in the treatment room would also be a practical issue, whose only solution would be reliant on a tracking or pointing system fitted to the treatment room. The HoloLens version of RAD-AR is intuitive to use and requires little user training. We believe that clinical applications as a tool for detection of large setup error, or detection of body shape changes larger than 2 cm between CT planning scan and treatment time is achievable for the HoloLens version.

User evaluation of the AR patient education tool was overall positive. Ease of visualization and quality of graphics content was rated superior to the corresponding leaflet version. Although the size of the sample of users is not large enough to draw definitive conclusions, interest and appreciation for the AR tool emerged in our studies. The field of view in the HoloLens was considered too narrow (a well known problem ("This is how Microsoft's HoloLens will address its biggest flaw," 2017)) that will likely be addressed in new versions of the device). Some users suggested that, if the hardware was lighter and with a larger field of view, using an AR tool instead of a diagram on paper would benefit elder patients especially as they often struggle to understand diagrams. A patient education tool would be implemented on more than one HMDs to be used collaboratively by the radiotherapy practitioner, explaining the treatment, and patients. Better understanding of their treatment would be beneficial, as it is likely to increase adherence to treatment preparation requests.

User evaluation of the AR tool for plan evaluation was also overall positive and very similar to user evaluation of the patient education tool on similar statements. Only the graphical representation of isodose surfaces and PTV was rated better on the AR tool to that of a 2D display for two users, and worse for three users; this is possibly due to high acquaintance of the users with dose and PTV visualization on 2D displays. Also for the plan evaluation tool the field of view of the HoloLens was considered too narrow. The size of the sample of users is too small to draw definitive conclusions, but indications of interest in utility of AR applications to radiotherapy emerged. Feedback from the two radiation oncologists was almost identical and overall more positive than feedback from the three medical physicists. Comments from three users pointed out a potential positive impact on a better understanding of complex cases, possibly using both AR and 2D display visualization to complement each other. A radiation oncologist suggested use of gaming controls for data navigation, the solution the authors intend to develop to make data navigation user friendly and intuitive. Clinicians also appreciated the possibility to increase the functionalities of RAD-AR (thanks to the portability requirement that guided the whole development process). Including several users to share a simultaneous view of the AR scene, while still seeing the real scene and other users, allowing in this way natural interaction with other radiotherapy professionals, was considered as a major future improvement to be implemented. Commercial applications to IGRT were also suggested by the senior clinician, e.g. implementation in RAD-AR of a tool to help understanding of CBCT data acquired at treatment time and comparison with planning CT data, exploiting multi-user interaction and intuitive perception of geometric features.

7.3 Conclusions

The scientific work presented in this thesis is to our knowledge the first study of possible applications of AR touching three of the main elements of radiotherapy - treatment planning, treatment delivery, and patient education - based on a coherent software framework.

In the literature review we found that at the beginning of this research project there had been no studies based on consumer electronics devices, as all existing studies were based on highly specialised or very expensive hardware. One of the outcomes of our work was the development of RAD-AR on consumer hardware platforms instead of highly specialised or very expensive devices. RAD-AR allows great flexibility in terms of portability to all main consumer electronics devices with AR capabilities. In that sense the very development of RAD-AR with a uniform design philosophy addresses part of the conclusions of the literature review.

When considering a broader range of AR applications, a second point identified from reported AR studies based on consumer electronics devices, indicated the possibility of achieving the accuracy and precision of registration needed for radiotherapy. The applications developed with RAD-AR have investigated this, including the accuracy and precision of the underlying self-tracking/camera-pose technologies and geometric fidelity of AR content representation.

Re-visiting our research hypothesis (section 1.3, reported as italic text in quotes in the rest of this section) we can claim that the basic statement and all of the three parts regarding treatment planning, treatment delivery, and patient education, have been validated. The basic statement in our research hypothesis:

> *"A user friendly AR software environment for applications to radiotherapy can be developed on low cost consumers AR platforms, without compromising on accuracy, robustness, usability, and portability to future platforms"*

has been shown. RAD-AR is a user friendly AR software environment for applications to radiotherapy*;* results of user feedback studies show that the system was reasonably comfortable and easy to use, and that the graphical representation of the radiotherapy elements considered was evaluated as comparable or superior to its 2D monitor counterpart, which is the current gold standard. RAD-AR was developed on low cost consumers AR platforms (iPad, costing £400 to £1000, and HoloLens, not cheap in its developer edition - £2700 - but prices for consumers are expected to drop significantly (“Microsoft does have plans to release Hololens for consumers,” 2017)).

The experimental quantitative investigation shows that it has been possible to develop RAD-AR “*without compromising on accuracy, robustness, usability, and portability to future platforms”*.

The first point of the research hypothesis, i.e. implementation of a

> *“clinical tool for patients positioning and setup errors detection”*

was the object of a quantitative study. Applicability of AR technology implemented on HMDs to some aspects of treatment delivery was shown to be feasible with current technology (detection of large setup errors and detection of patient body changes negatively affecting, and possibly invalidating, treatment outcome). Use as an independent patient setup tool could be realized, subject to improvement in hardware specifications, especially regarding the self-tracking aspects of HMDs.

The second point in our research hypothesis, i.e. implementation of an

> *“educational aid tool for radiotherapy practitioners to help explaining to patients some aspects of their radiotherapy treatment, and the importance of preparation for treatment, by visualizing their treatment, and demonstrating to patients e.g. the importance of compliance with instructions around bladder filling and rectal evacuation”*

was also demonstrated. Usability of AR to educate patient about their treatment was investigated and a user feedback experiment showed overall positive user evaluation of features on potential applications of the tool. When new advances in the technology will make available lighter HMDs, possibly with a larger field of view, such a tool could become part of current clinical practice. Most patients have little knowledge of internal anatomy or have little propensity to understand diagrams so they would benefit from an AR experience, shared with the radiotherapy professional, to understand their treatment. Assuming that better understanding of the treatment induces patients to follow with more accuracy the correct preparation procedure, AR could help to increase the chances of correct treatment outcome.

Finally, also the third point of our research hypothesis, i.e. implementation of

> “*a visualization aid for clinicians to enable a better understanding of 3D features of radiotherapy plans”*

was demonstrated and investigated with a user feedback experiment. User feedback was overall positive. Amongst suggestions received from user feedback studies, comments from the two radiation oncologists were very encouraging, as they could envisage commercial applications of RAD-AR, e.g. in the phase of IGRT treatments where a CBCT scan is acquired on the treatment couch immediately prior or during treatment and needs to be compared in a short period of time (a few minutes) to the planning CT scan; comparison of 3D features is a key point and an AR shared experience allowing radiographers and doctors to inspect the datasets would be highly beneficial.

Commercialization of AR systems for other medical disciplines has already started and is growing fast (Ma, Jain, & Anderson, 2014) (L. Chen et al., 2017). A spin-off company, HoloSurg3D (San Francisco, CA 94127, [21]) have launched RadHA, a HoloLens based application allowing surgeons to view radiology images projecting 3D images onto a real-world background. Claims made by the company (Courtier, 2017) match our view on AR applications in medicine in general and radiotherapy in particular. HoloSurg3D applications address surgical procedures, where the patient anatomy changes during the procedure; registration of AR content in that case poses additional problems. RAD-AR applications would instead aim to detect anatomical changes, and this would be a major simplification for underlying technical problems, foreseeing the possibility of commercial applications of RAD-AR. We believe that HMD platforms have very strong potential for application as a clinical patient set-up tool in the near future, acting as a competing system to commercial innovative systems ((Krengli et al., 2009), AlignRT, Vision RT, London, UK) costing in the range of $180,000 to $200,000.

AR user interfaces are starting to be considered a valid alternatives to the standard WIMP paradigm in other medical specialities (Issartel, Gueniat, & Ammi, 2014)(Katić et al., 2010). We share this view and we believe that AR will complement, and some case replace, WIMP interfaces in radiotherapy too.

Summarizing, based on the outcome of our research, our general view about AR application to radiotherapy is that it could help:

- radiotherapy practitioners to better inform/educate patients about their treatment;
- clinicians and other health professionals to understand complicated treatment details;

- to improve treatment delivery by making it faster, safer, and more efficient.

The research carried out fits in the research trend for AR applications to medicine, and to modern radiotherapy technology, relying always more on the availability of a large amount of 3D imaging data needing innovative visualization techniques to be exploited in the best possible way to deliver high quality patient care.

7.4 Future Work

Proposed further developments include the following aspects:

1. Larger studies across multiple hospital sites with increased sample size to draw statistically sound conclusions could be realized with reasonable effort, as user feedback experiments with sample size statistically relevant (Park & Jung, 2009) can be performed spending only a few hours on each site.
2. User feedback studies with patient using the AR tools (subject to ethical approval).
3. Consequent follow-up studies to understand the longer term outcome on patients following the introduction of AR tools.
4. Development and commissioning of a clinical tool based on the HoloLens version of RAD-AR for detection of large setup errors and discrepancy of patient body shape between planning CT scan and treatment time.
5. Deployment and investigation of RAD-AR on other emerging AR platforms such as Meta 2 ("Meta Company," 2018), Magic Leap ("Magic Leap," 2018), and porting to other SDKs, e.g. the new Apple ARKit. It would be interesting to compare devices designed using different technology to implement AR content rendering: diffraction gratings for HoloLens ("AR/MR Combiners Part 2 – Hololens | Karl Guttag on Technology," 2017) and Meta 2, digital lightfield for Magic Leap ("Magic Leap," 2018). The field of view appears less of an issue for other devices, c.f. 35˚ for HoloLens, 90˚ for Meta 2 (Pulli, 2017), and Magic Leap also claiming a larger field of view than the HoloLens but this is debated ("Magic Leap," 2018)("The Science Behind Augmented Reality Hardware," 2018). Magic Leap will be distributed with handheld controls, and this would address comments received in our user feedback experiment of the plan evaluation tool. Apple acquired augmented reality headset start-up Vrvana for $30M ("Apple acquired augmented reality headset startup Vrvana," 2017), and is

reported to release a standalone AR headset for 2019 ("Apple reportedly readying standalone AR headset," 2018). ARKit was released in mid 2017 and shows potential to improve accuracy over other AR SDKs ("ARKit demo: accurate room measurement," 2018). The most recent release (September 2017) is based on iOS 11 and exploits the new TrueDepth Camera fitted on iPhone X. Due to the release date we did not have the opportunity to port RAD-AR to ARKit. Building an iOS version of RAD-AR based on Apple ARKit will then have two possible outcomes:

- positive impact on accuracy, precision, and faithfulness of virtual content placement by deployment to a device featuring the TrueDepth Camera ("How TrueDepth could make Apple's AR headset actually work," 2018)
- straightforward portability of RAD-AR to the standalone AR headset that Apple should release in 2019 ("Apple May Unveil Standalone AR Headset in 2019," 2018); experimental investigation and comparison with the HoloLens version (Apple vs. Microsoft is always an interesting challenge ("Can Microsoft keep up with Apple in the race for AR/VR," 2018)).

6. Volume rendering on the HoloLens; this is one of the aspects that we did not have the opportunity to investigate in depth; only a rudimentary version was implemented and tested; user feedback was positive and showed interest in providing this type of functionality in an evolved version of RAD-AR. Recent developments have occurred and more information is available from Microsoft ("Volume rendering," 2017).

7.5 Final Remark

Based on the work conducted during this research and the activity reported elsewhere, there is little doubt that AR will become a useful tool in a hospital with many potential applications. We are convinced that in the Radiotherapy treatment room there are real benefits in the future for both clinicians and patients, with AR contributing to successful treatment outcomes.

Appendix

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Betsi Cadwaladr
University Health Board

University of Chester

Thornton Science Park

RAD-AR

RADiotherapy – Augmented Reality

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INTRODUCTION

To assist different radiotherapy treatment aspects, we built an augmented reality application (RAD-AR) for widely available hand held consumer tablet devices and for the holographic visor Microsoft HoloLens, using the Unity3D (Unity Technologies, 5.6) development platform, the VuforiaTM (PTC) AR library (for tablets) and the Unity HoloLens SDK (for HoloLens).

OBJECTIVES

We identified three potential types of application for our AR system.

Visualization of medical information for clinicians and other radiotherapy professionals

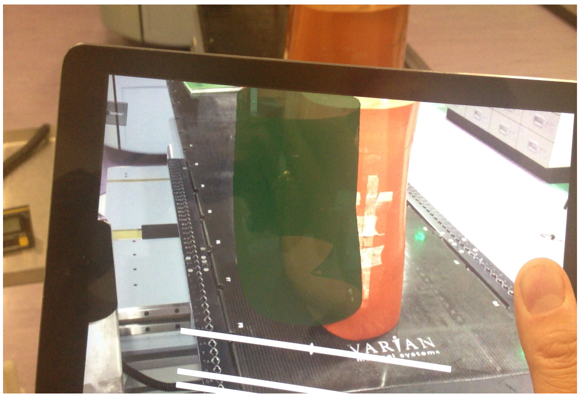
CT scans, MRI scans and radiotherapy treatment dose distributions are generally presented in 2D on computer displays. Our system enables a more intuitive and natural navigation and visualization of patient's 3D datasets and treatment plans.

Patient positioning for radiotherapy treatment

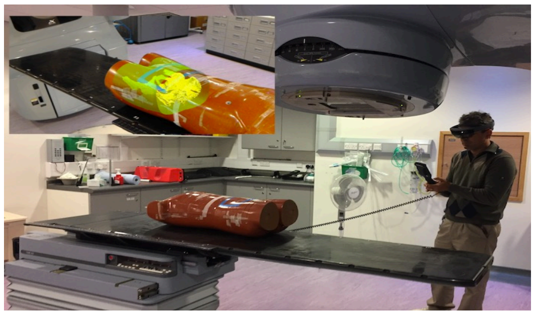
Patient positioning is conventionally based on alignment of a set of laser lights to a number (usually three) of permanent ink marks put on the patient skin when the planning CT scan is acquired. It is assumed as an approximation that the patient body behaves like a rigid object and that the patient body shape has not changed since the time when the planning scan was acquired. Our system could be used to reproduce the patient position and body shape from CT scanner to the linac, by displaying the 3D patient body outline as virtual content registered in a consistent way to the physical environment of the CT scanner and the linac.

Patient treatment education

The patient is explained the importance of carrying out preparation procedures (e.g. having an enema and drinking water following a prescribed schedule) prior to treatment. The negative impact that an improper preparation could have on the treatment outcome can be illustrated using AR.



iPad version of RAD-AR



HoloLens version of RAD-AR

EXPERIMENTS

An experimental evaluation of reproducibility of patient positioning using radar has been performed using an anthropomorphic phantom deigned for radiotherapy quality control (RANDO, RSD Inc.) We performed a preliminary study of precision for both the iPad and the HoloLens versions of RAD-AR.

The CT outline of the RANDO was positioned on the treatment couch as AR content. The physical phantom was then aligned to its AR outline. The couch position was recorded. Vertical, horizontal, longitudinal and angular shifts were applied to the couch. The RANDO was then realigned to its AR outline by moving the couch.

The spreads of couch positions are measurement of precision (precision in physics quantifies the reproducibility of repeated measurements results). Precision of couch positions was 1 cm for the iPad and 1.5 cm for the HoloLens. Precision of couch angle was 3° for the iPad and 4° for the HoloLens.

Initial feedback from clinicians that have tried RAD-AR as a visualization tool and as a patient education tool is encouraging.

CONCLUSIONS

The tool in its current implementation can aid to pick up large set up errors, such as those that can occur when applying incorrect couch moves or using incorrect, previous tattoos for set up.

Precision of the iPad implementation of RAD-AR is higher than precision for the HoloLens version. This can be explained considering that in the iPad implementation, built on Vuforia, self-tracking is marker based and the AR content was placed close to the marker at approximately 30 cm (we used a cylinder marker – 5 cm radius, 12 cm height). For the HoloLens self tracking is based on environment mapping and the AR content is at a greater distance from the main tracking elements (walls, floor).

Further work is required to analyze the minimum errors that can be picked up and will be operator dependent. We also envisage further work to introduce the light field and a facility to look into the body to visualize how close a particular organ at risk is to the irradiated volume or treatment target. At this point a role in adaptive radiotherapy could be envisaged and of course it would enhance the experience as a tool to explain to patients the radiotherapy process and the importance of complying with instructions around bladder filling and rectal suppositories.

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Figure 75 Poster Presented at Cyberworlds International Conference (University of Chester, UK, September 2017, best poster award).

Glossary

AR	Augmented Reality
CBCT	Cone-Beam Computed Tomography
CT	Computed Tomography
CTV	Clinical Target Volume
HMD	Head-Mounted Display
IGRT	Image Guided Radiotherapy
IMRT	Intensity-Modulated Radiation Therapy
LINAC	Linear accelerator
MRI	Magnetic Resonance Imaging
MU	Monitor Unit - a measure of machine output from a clinical accelerator for radiation therapy
PTV	Planning Target Volume
Shader	computer programs that calculate rendering effects on graphics hardware
SPECT	Single-Photon Emission Computed Tomography
US	Ultrasound
VR	Virtual Reality

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